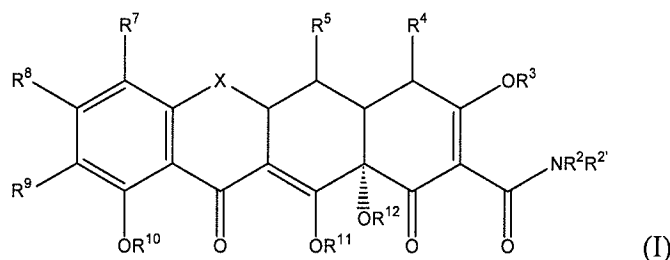


**AMENDMENTS TO THE CLAIMS:**

**Listing of Claims:**

This listing of claims will replace all prior versions of the claims and listing of the claims in the application:

1. **(Currently Amended)** A method for treating a subject for a disease treatable by modulation of RNA (DTMR) associated with splicing of nuclear RNA, comprising: administering to said subject an effective amount of a tetracycline compound of formula (I):



wherein

$R^2$ ,  $R^{2'}$ ,  $R^{4'}$ , and  $R^{4''}$  are each independently hydrogen~~[[,]]~~ or alkyl, ~~alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;~~

$R^3$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each hydrogen, ~~alkyl, alkenyl, alkynyl, substituted carbonyl, or a pro-drug moiety;~~

$R^4$  is  $NR^{4'}R^{4''}$ , ~~alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;~~

$R^5$  is hydroxyl, ~~hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;~~

$R^6$  and  $R^6'$  are each independently ~~hydrogen, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;~~

$R^7$  is ~~hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, substituted alkenyl, substituted alkynyl, arylsubstituted phenyl, substituted or unsubstituted furanyl, alkoxy,~~

~~alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, or aminoalkyl, heterocyclic, thionitroso, or  $(CH_2)_{0-3}NR^{7e}C(=W')WR^{7a}$ ;~~

~~$R^8$  is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or  $(CH_2)_{0-3}NR^{8e}C(=E')ER^{8a}$ ;~~

~~$R^9$  is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or  $(CH_2)_{0-3}NR^{9e}C(=Z')ZR^{9a}$ ; and~~

~~$R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}$ , and  $R^{8f}$  are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;~~

~~$R^{13}$  is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;~~

~~E is  $CR^{8d}R^{8e}$ , S,  $NR^{8b}$  or O;~~

~~E' is O,  $NR^{8f}$ , or S;~~

~~W is  $CR^{7d}R^{7e}$ , S,  $NR^{7b}$  or O;~~

~~W' is O,  $NR^{7f}$ , or S;~~

~~X is  $CHC(R^{13}Y'Y)$ ,  $CR^{6'}R^6$ , S,  $NR^6$ , or O;~~

~~$Y'$  and  $Y$  are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;~~

~~Z is  $CR^{9d}R^{9e}$ , S,  $NR^{9b}$  or O; and~~

~~$Z'$  is O, S, or  $NR^{9f}$ , or a pharmaceutically acceptable salt, ester or enantiomer thereof, with the proviso that said tetracycline compound is not tetracycline;~~

such that said DTMR associated with splicing of nuclear RNA is treated, wherein said DTMR associated with splicing of nuclear RNA is spinal muscular atrophy, and further

wherein said effective amount is effective to modulate splicing of said subject's nuclear RNA.

2.-36. (Canceled)

37. (Previously Presented) The method of claim 1, wherein  $R^2$  and  $R^{2'}$ ,  $R^8$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are each hydrogen, X is  $CR^6R^{6'}$ , and  $R^4$  is  $NR^{4'}R^{4''}$ , wherein  $R^{4'}$  and  $R^{4''}$  are each methyl.

38. (Canceled)

39. (Currently Amended) The method of ~~claim 38~~ claim 37, wherein  $R^7$  is substituted or unsubstituted ~~aryl~~ furanyl.

40. (Currently Amended) The method of ~~claim 39~~ claim 37, wherein  $R^7$  is substituted or unsubstituted phenyl.

41. (Canceled)

42. (Currently Amended) The method of ~~claim 41~~ claim 40, wherein said substituted phenyl is substituted with one or more substituents and further wherein said substituents are each independently alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, cyano, amino, acylamino, amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, aryl or heterocyclic moiety.

43. **(Currently Amended)** The method of ~~claim 38~~claim 37, wherein R<sup>7</sup> is substituted or unsubstituted alkenyl.

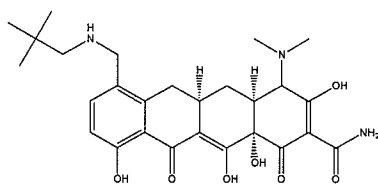
44. **(Currently Amended)** The method of claim 37, wherein R<sup>7</sup> is substituted alkynyl or unsubstituted heteroaryl and R<sup>9</sup> is alkyl.

45. **(Currently Amended)** The method of ~~claim 36~~claim 37, wherein R<sup>7</sup> is dialkylaminoacyl.

46. **(Currently Amended)** The method of ~~claim 45~~claim 37, wherein R<sup>9</sup>R<sup>7</sup> is alkylaminoaminoalkyl.

47.-56. **(Canceled)**

57. **(Previously Presented)** The method of claim 1, wherein said tetracycline compound is:



, or a pharmaceutically acceptable salt thereof.

58. **(Canceled)**

59. **(Previously Presented)** The method of claim 1, wherein said modulation of splicing increases splicing of RNA.

60. **(Previously Presented)** The method of claim 1, wherein said modulation of splicing decreases splicing of RNA.

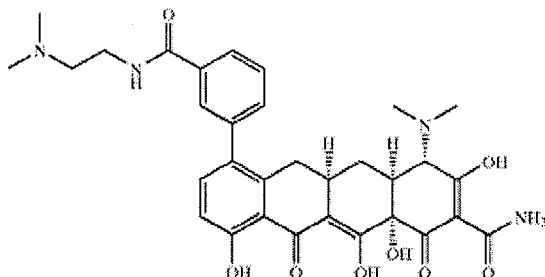
61. **(Canceled)**

62. **(Previously Presented)** The method of claim 1, wherein said subject is a mammal.

63. **(Previously Presented)** The method of claim 62, wherein said mammal is a human.

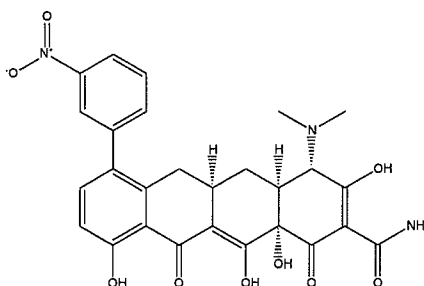
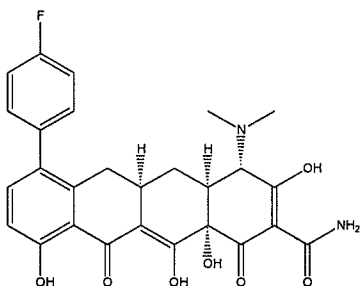
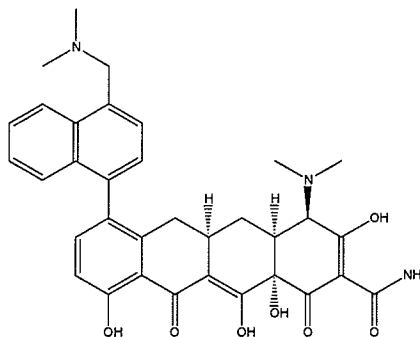
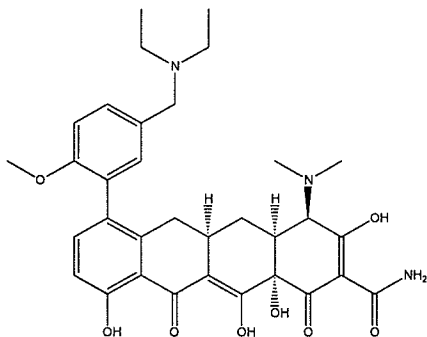
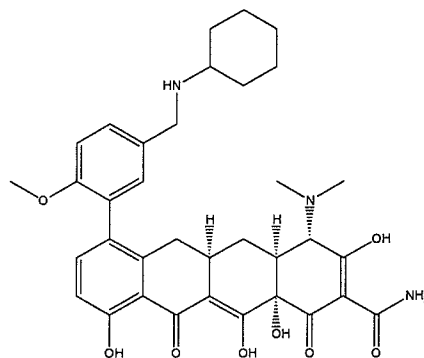
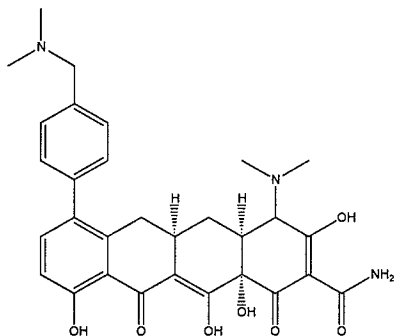
64. **(Previously Presented)** The method of claim 1, wherein said modulation of splicing is activation of cryptic splice sites, silencing of consensus splice sites, silencing of exonic or intronic splicing enhancers (ESEs or ISEs), silencing of exonic or intronic splicing silencers (ESSs or ISSs), alteration of the binding or a component of the splicing machinery to the RNA, or the affecting of intermolecular interactions between components of the splicing machinery.

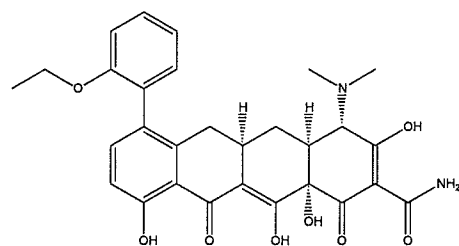
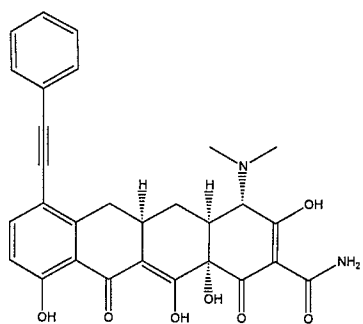
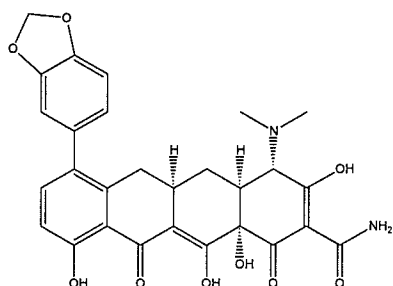
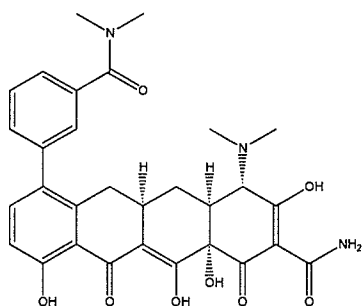
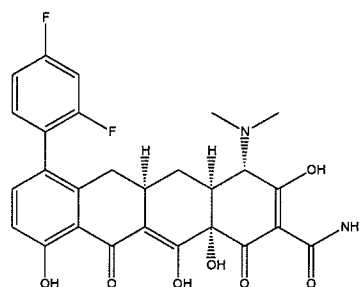
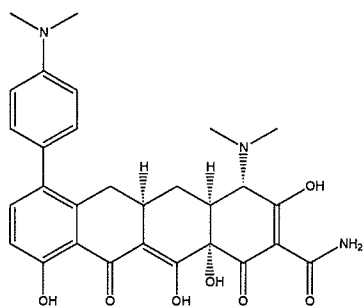
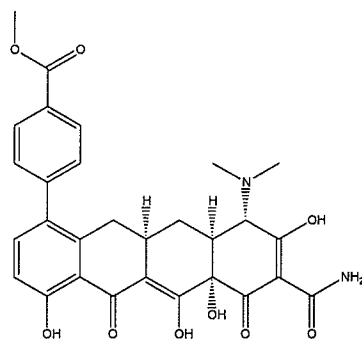
65. **(Previously Presented)** The method of claim 1, wherein said tetracycline compound is:

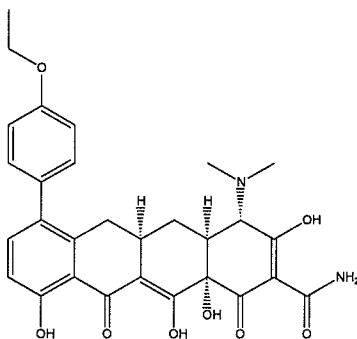
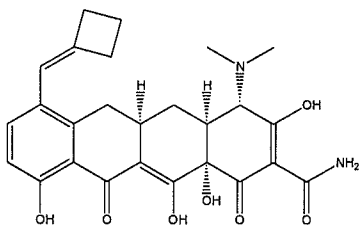
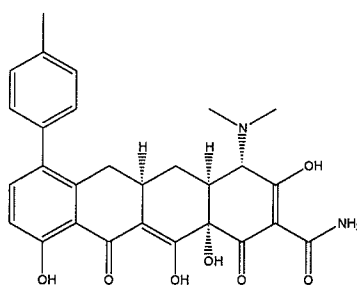
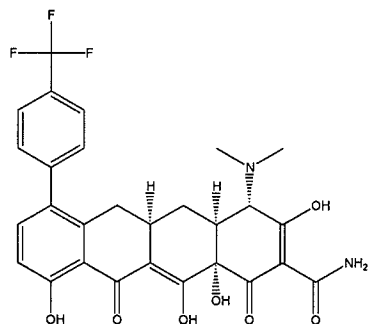
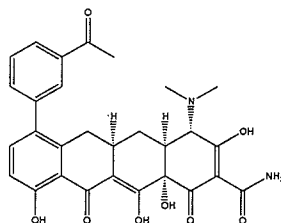
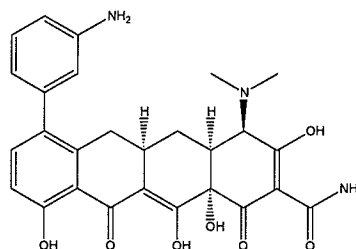
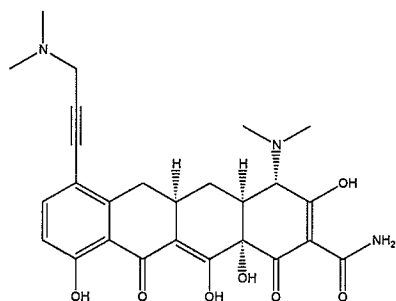
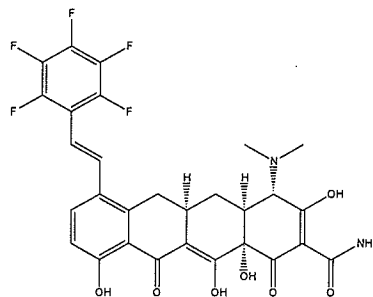
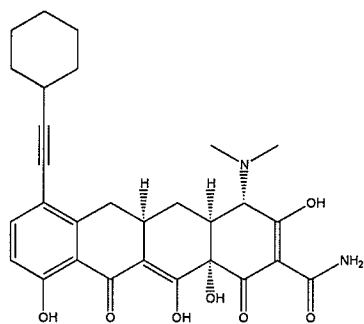


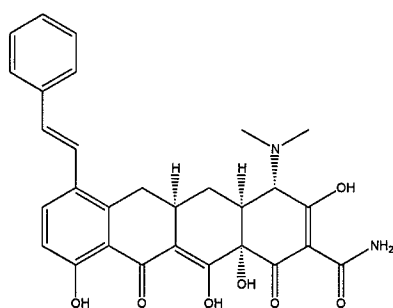
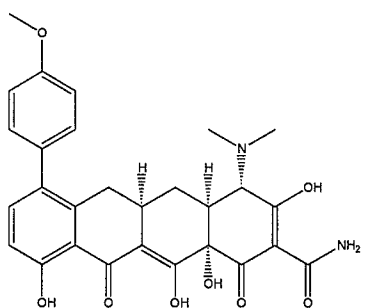
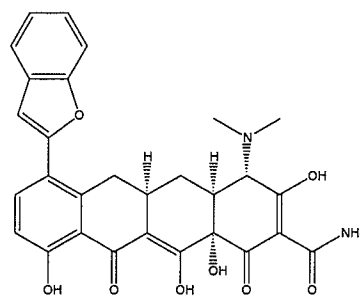
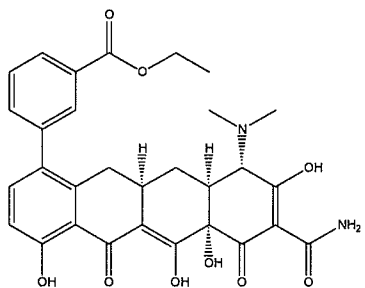
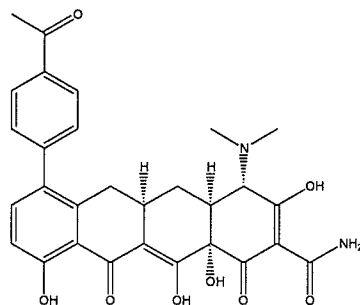
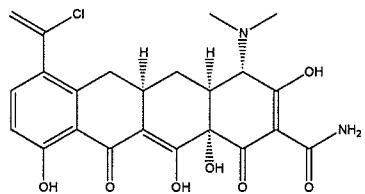
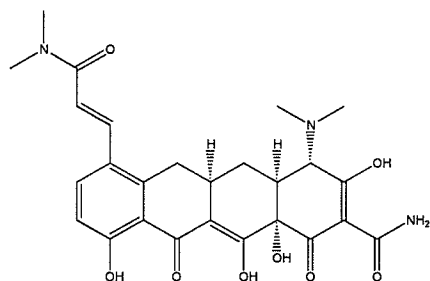
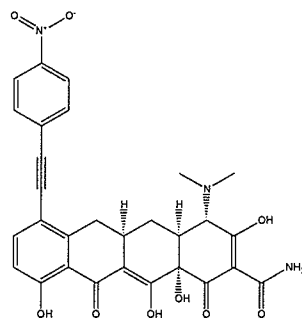
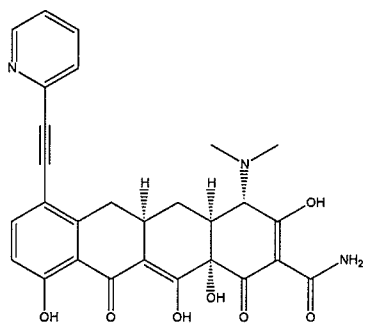
, or a pharmaceutically acceptable salt thereof.

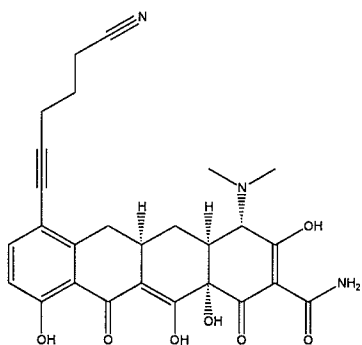
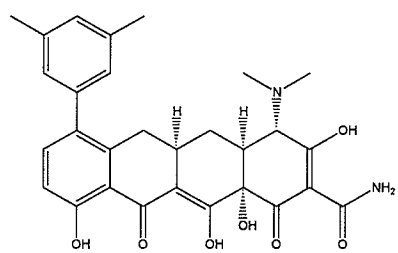
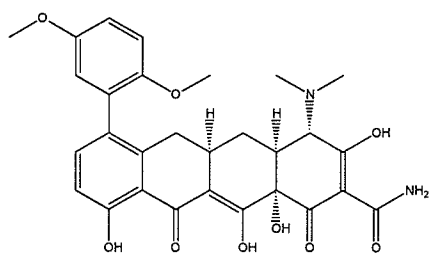
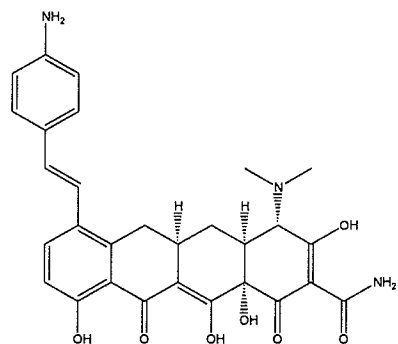
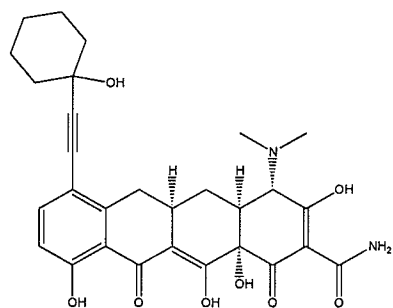
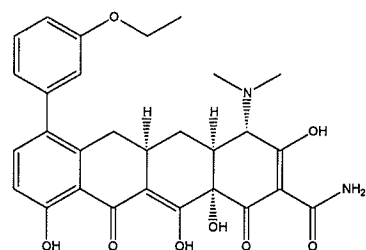
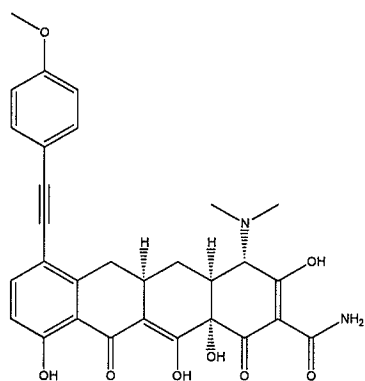
66. (New) A method for treating a subject for a DTMR associated with splicing of nuclear RNA, comprising: administering to said subject an effective amount of a tetracycline compound; wherein said tetracycline compound is a tetracycline compound selected from the group consisting of:

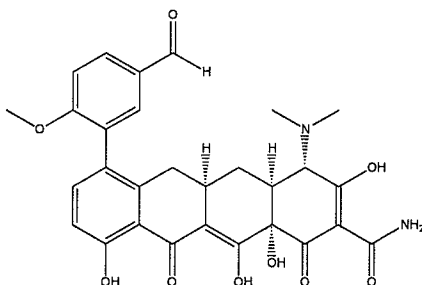
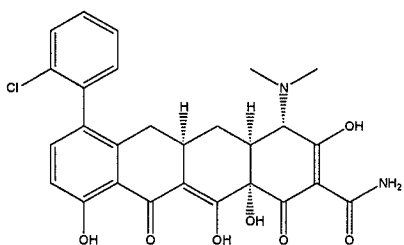
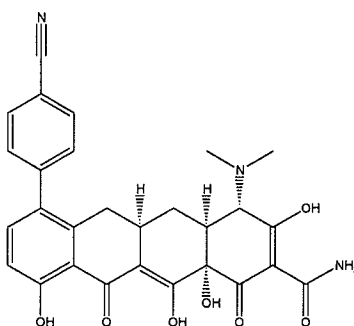
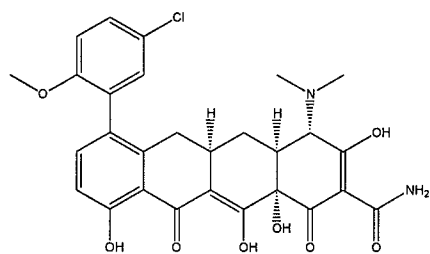
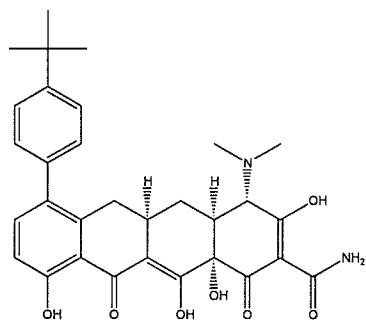
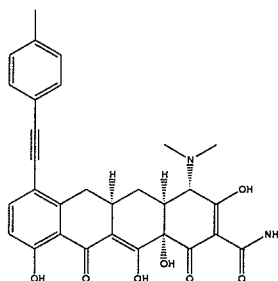
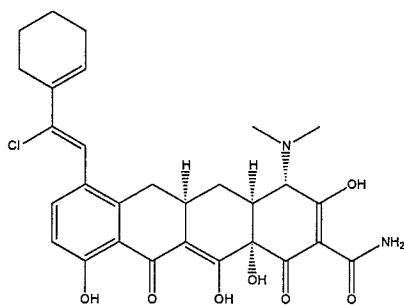
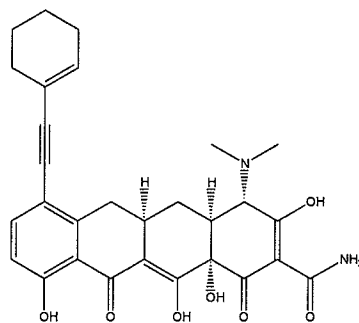
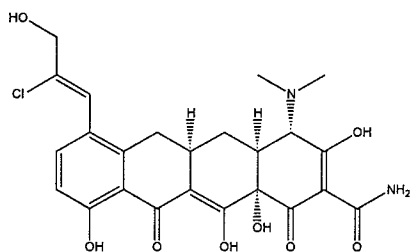


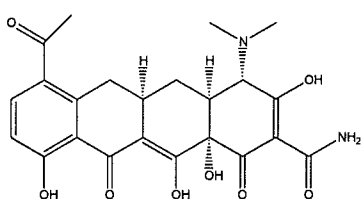
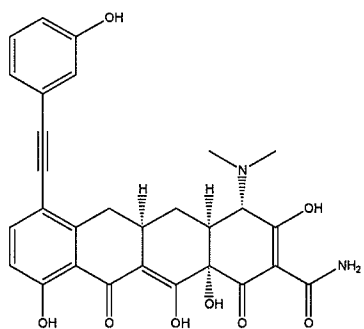
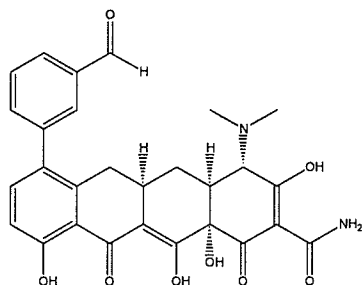
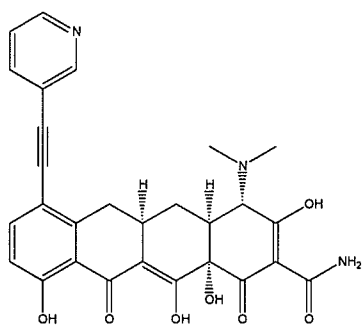
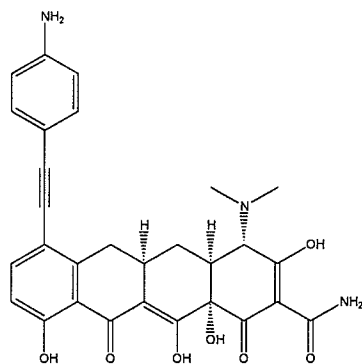
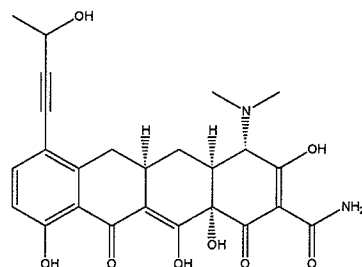
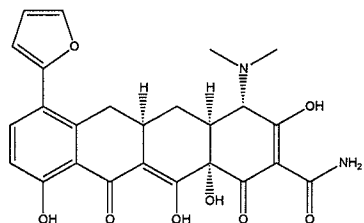


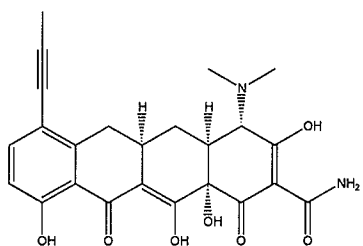
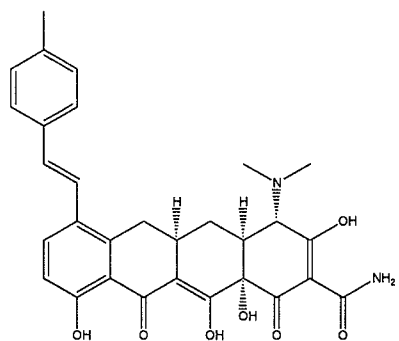
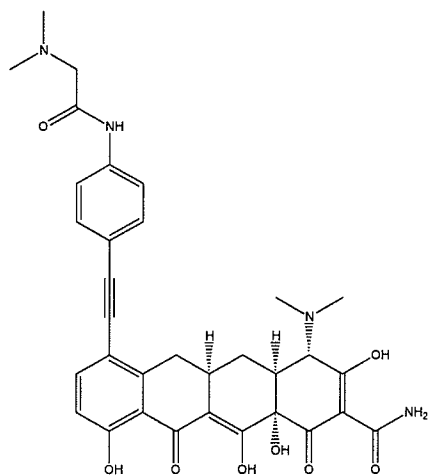
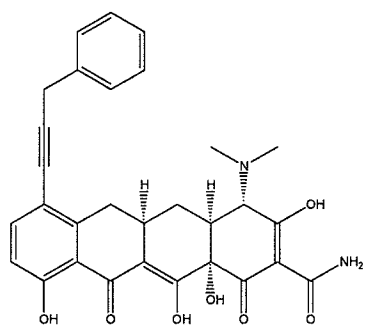
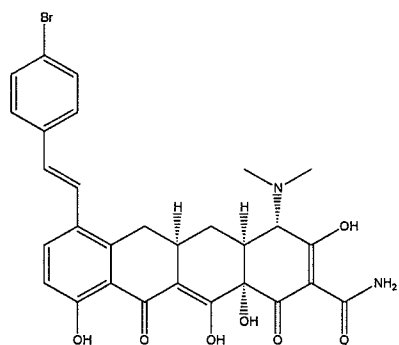
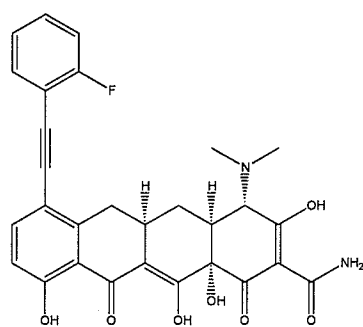
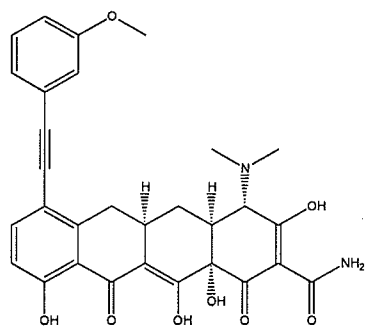


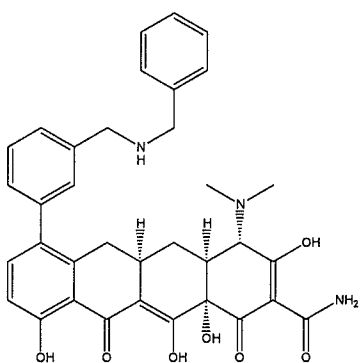
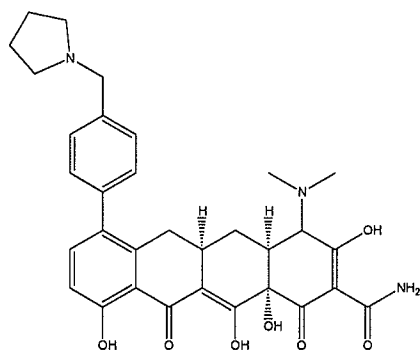
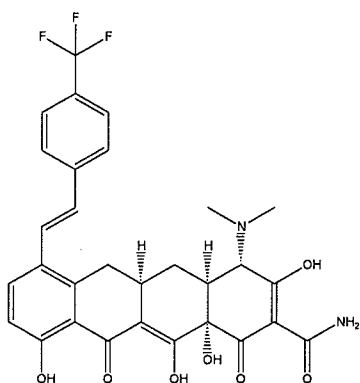
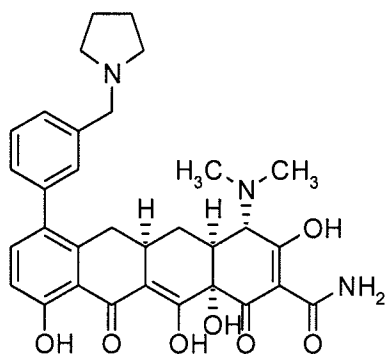
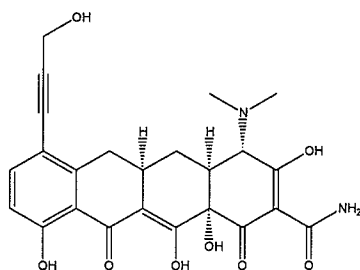
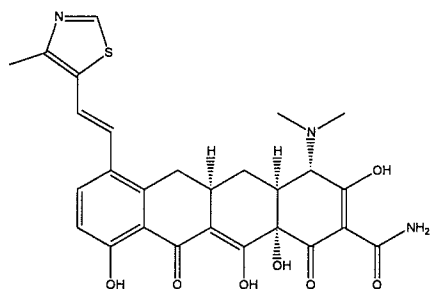
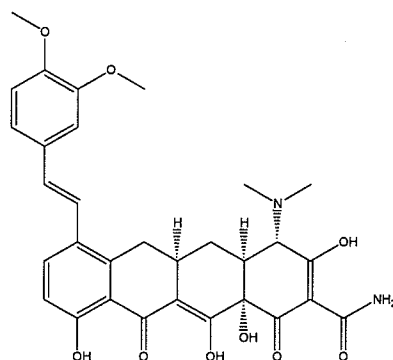
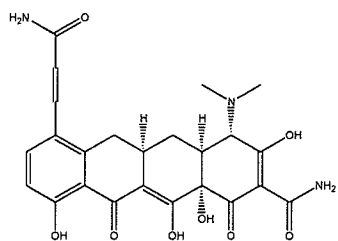


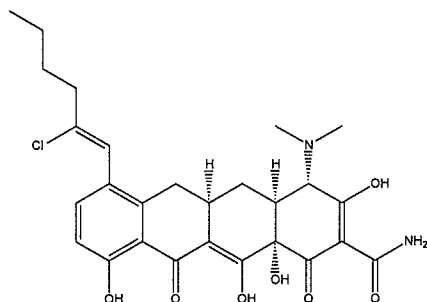
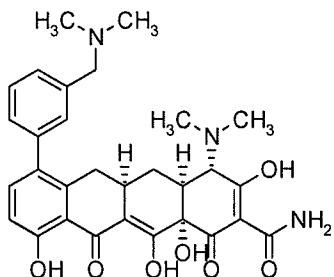
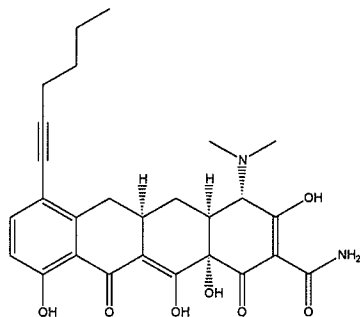
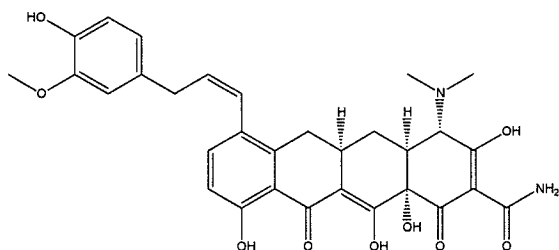
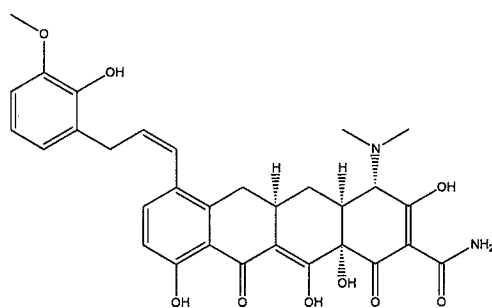
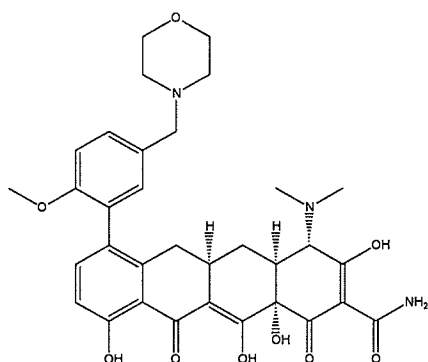
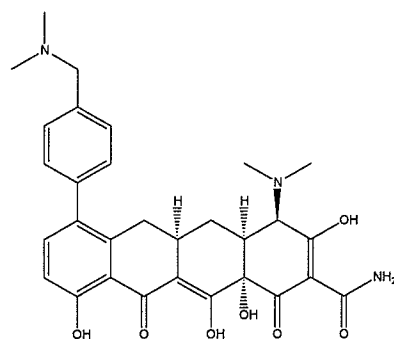
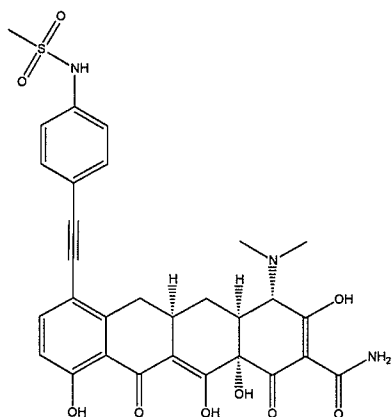


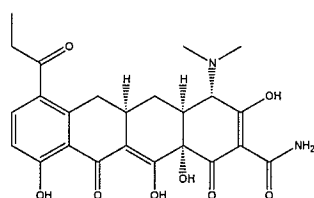
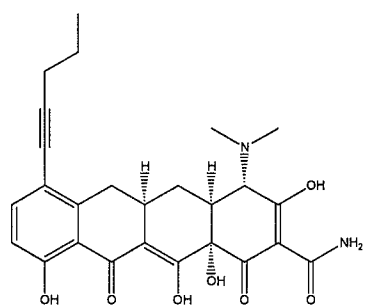
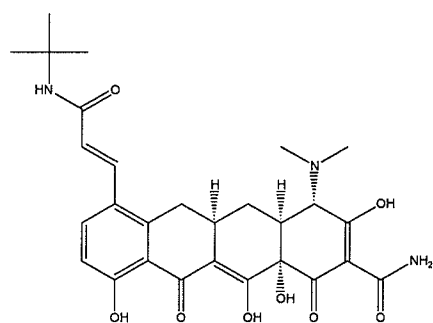
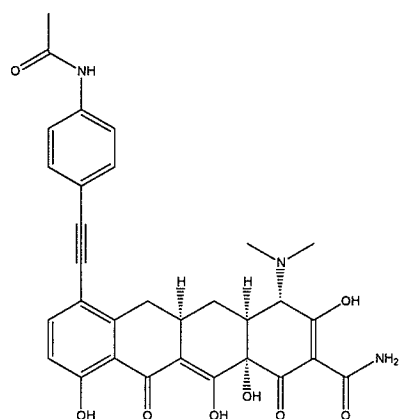
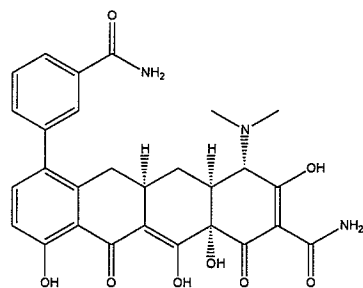
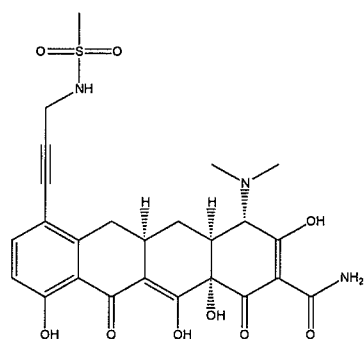


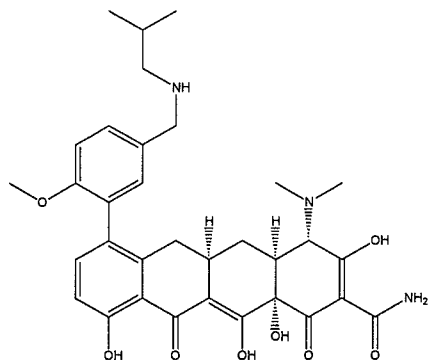
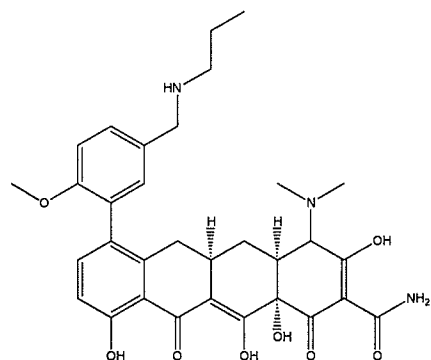
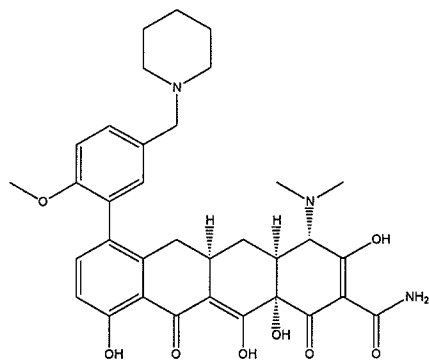
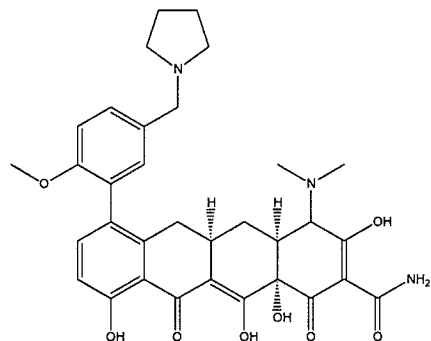
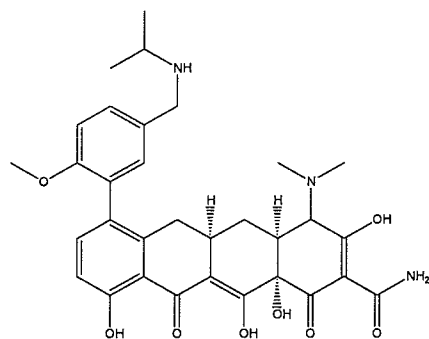
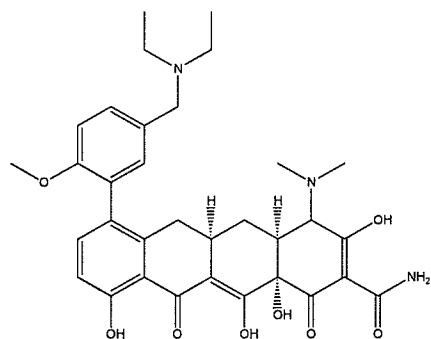
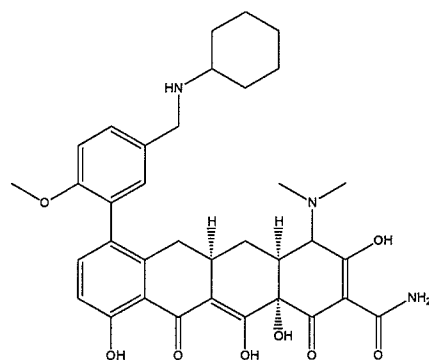


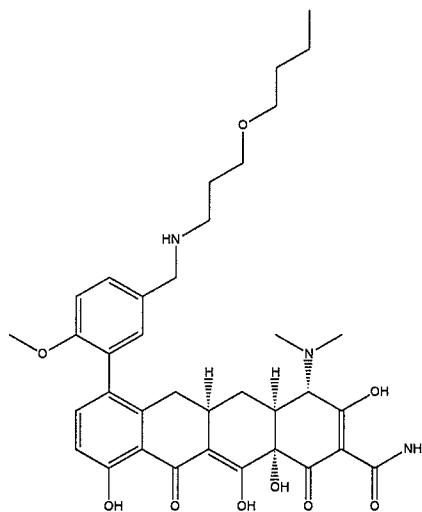
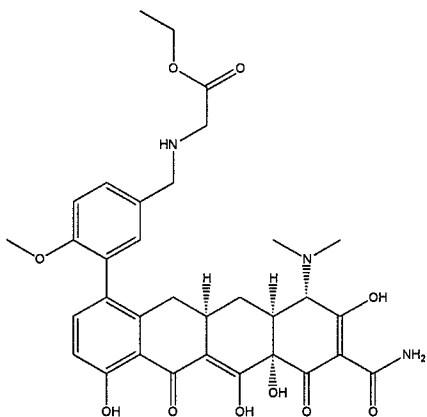
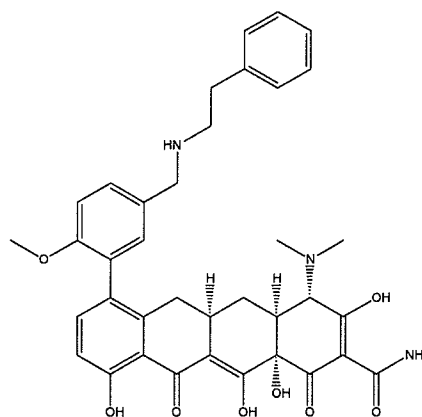
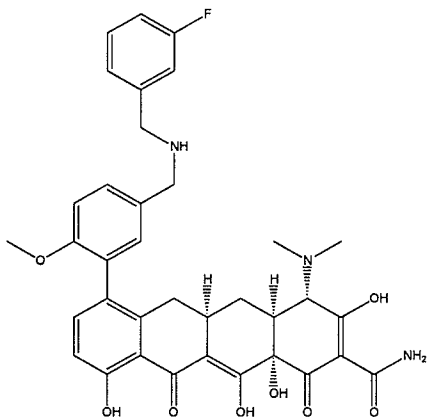
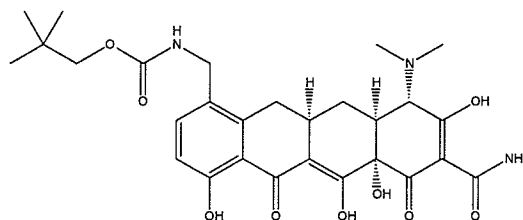
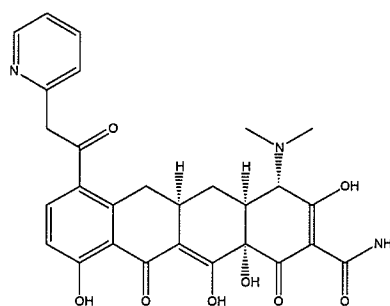
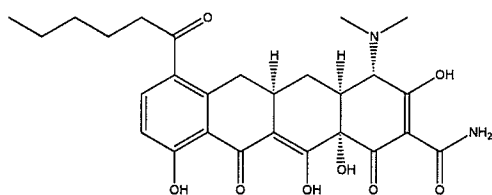


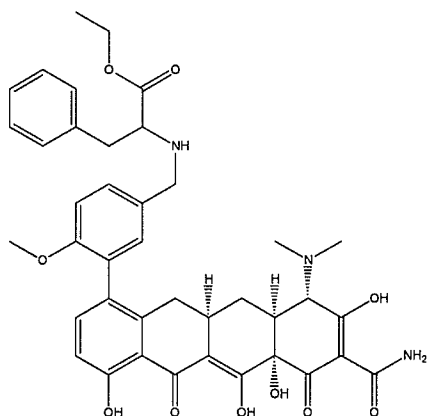
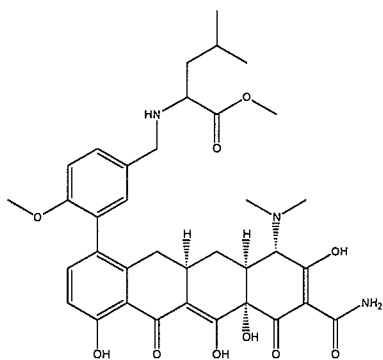
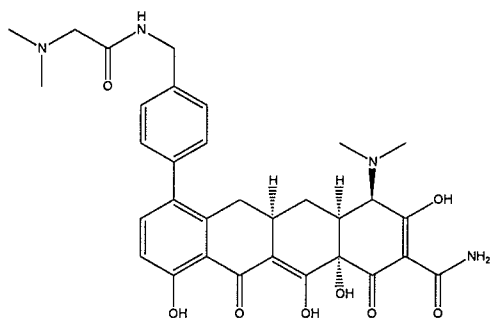
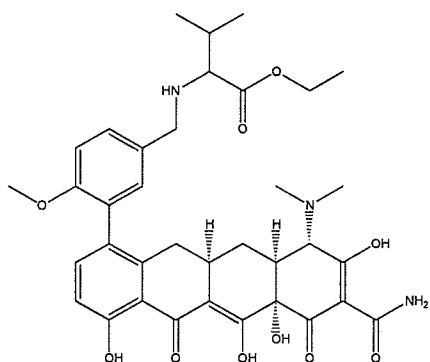
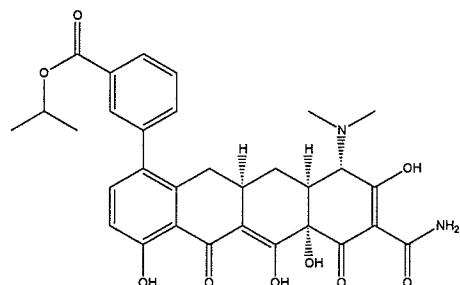
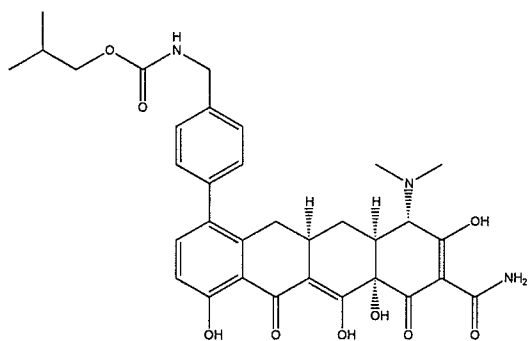
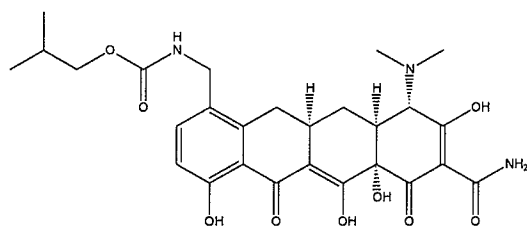
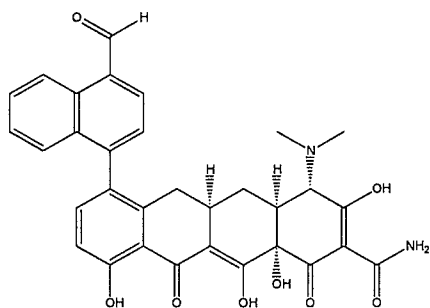


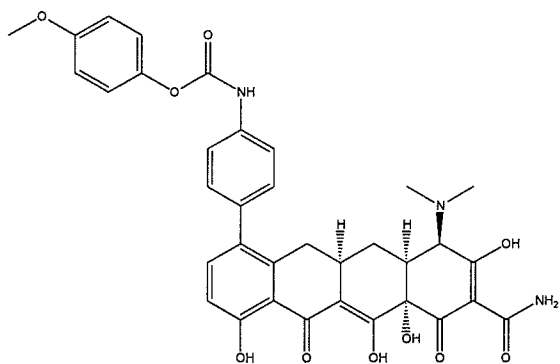
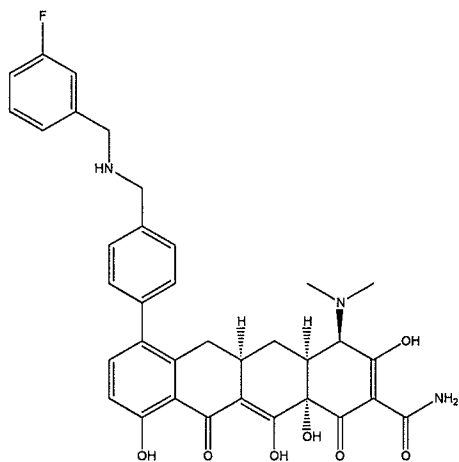
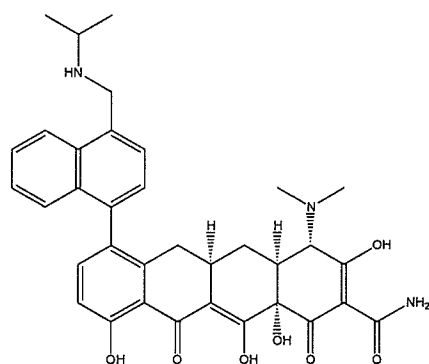
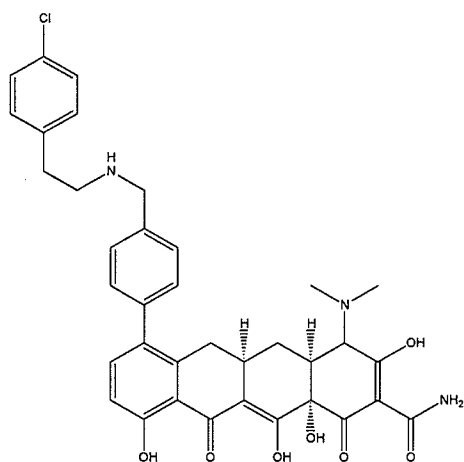
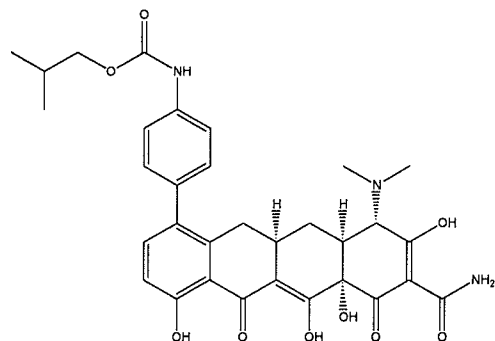
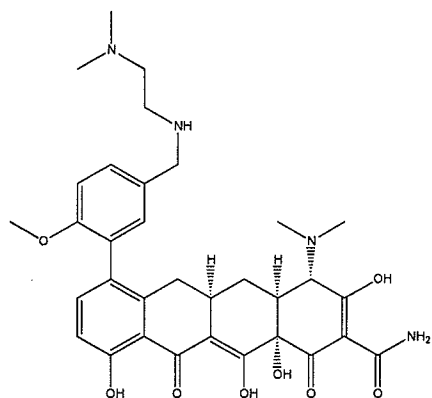


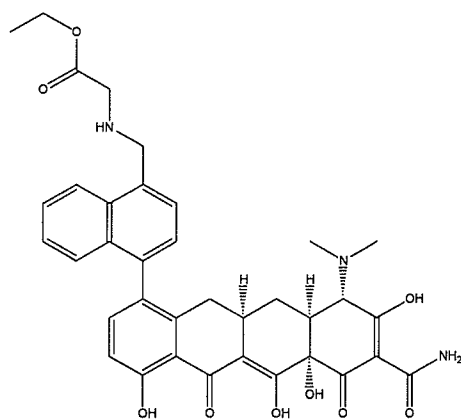
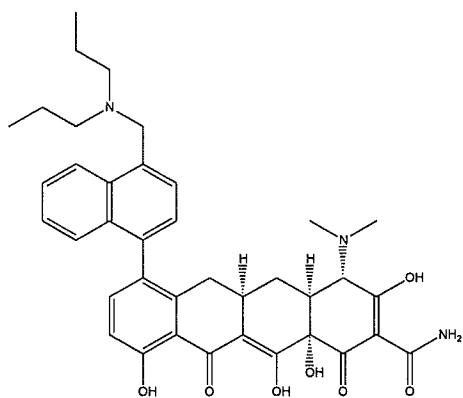
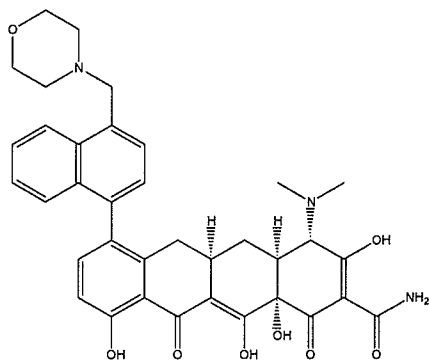
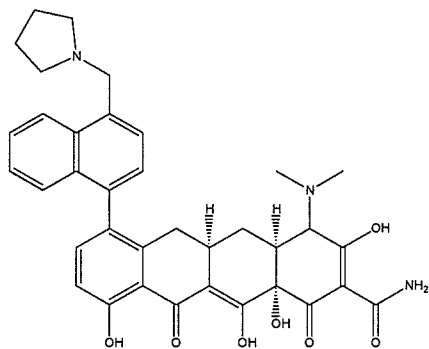
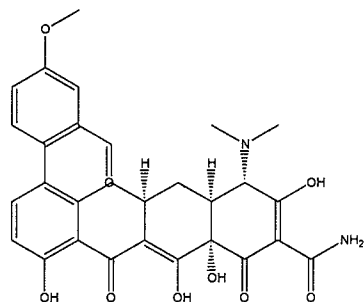
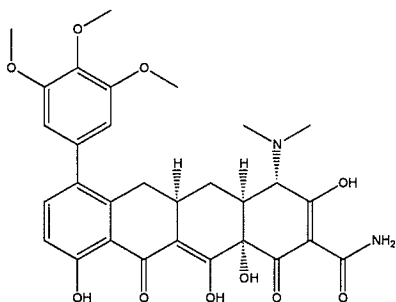
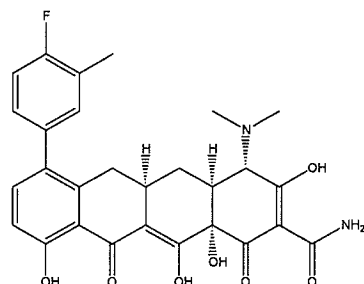
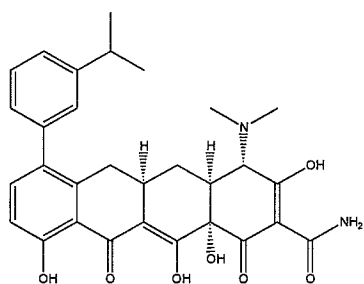


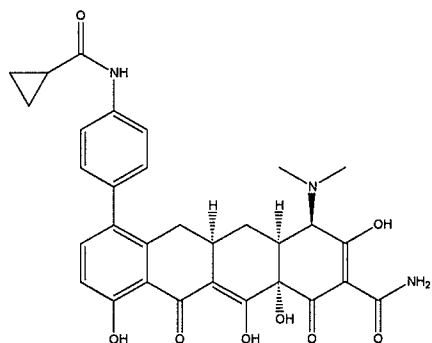
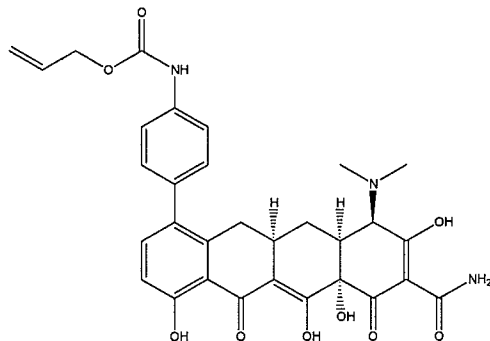
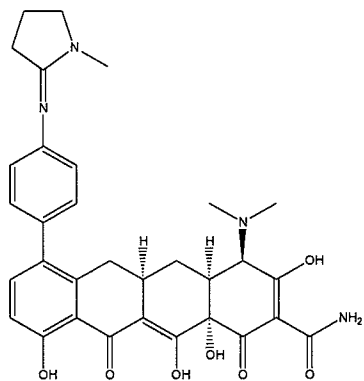
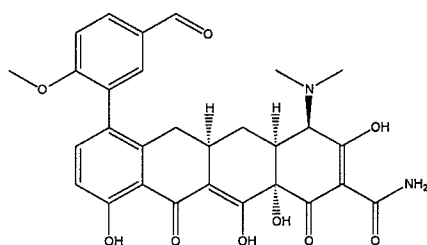
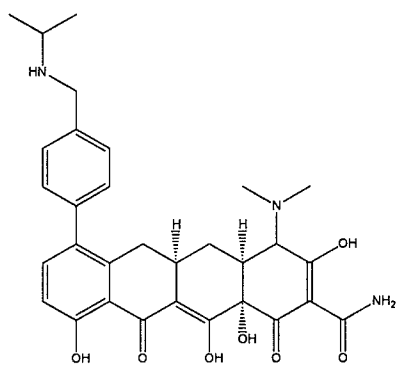
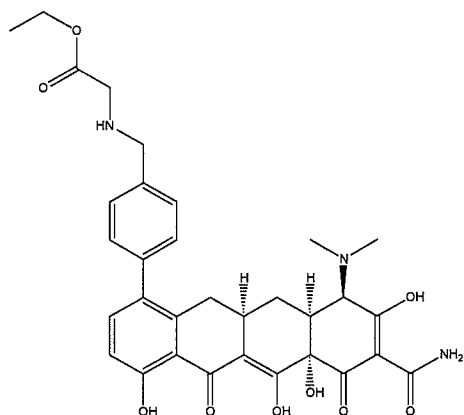
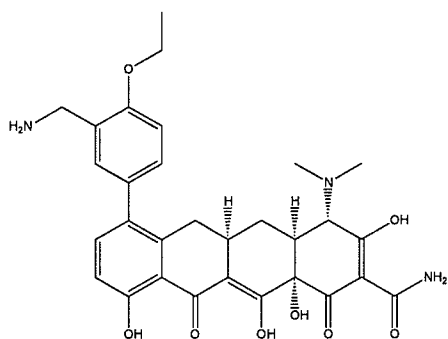


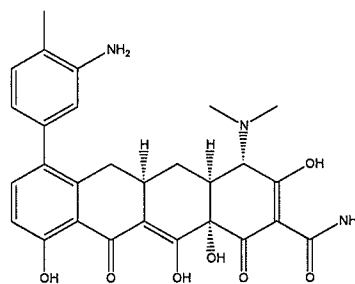
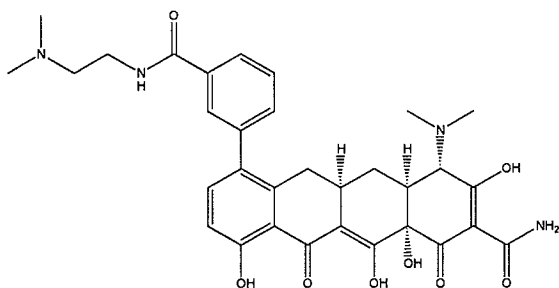
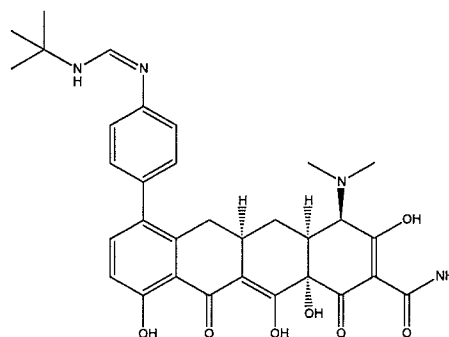
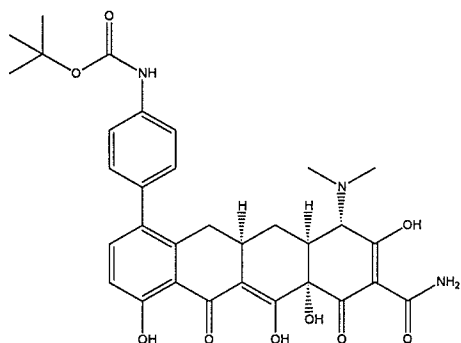
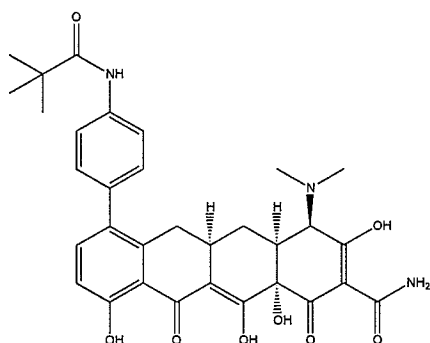
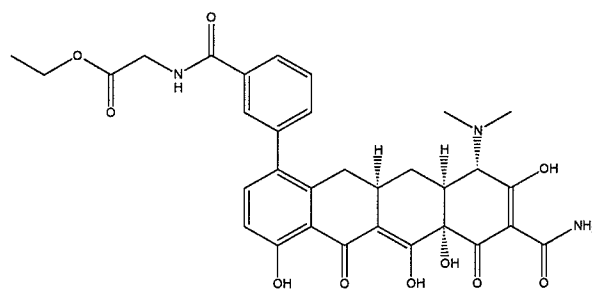
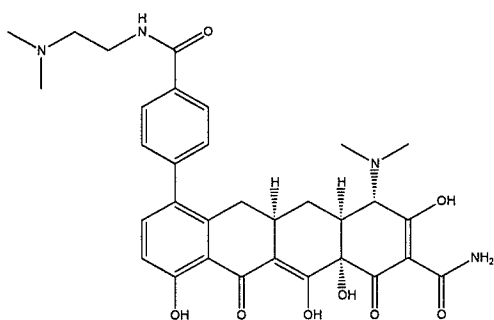


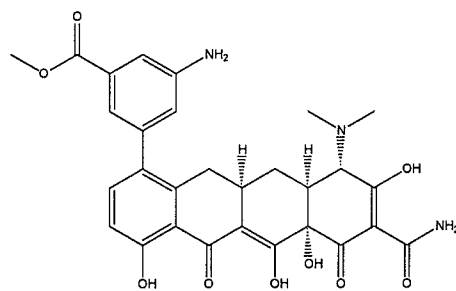
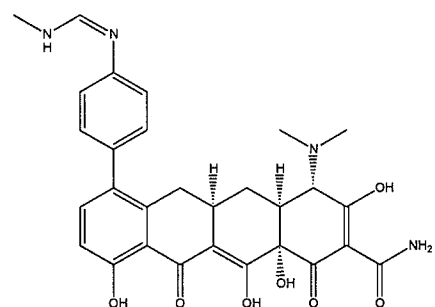
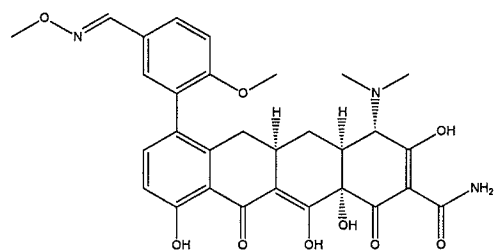
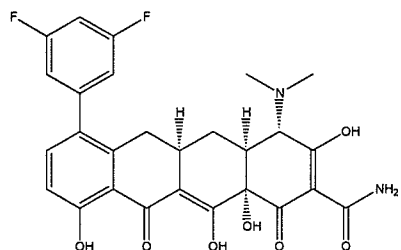
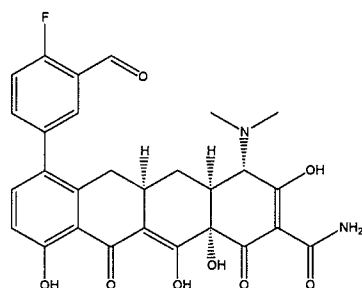
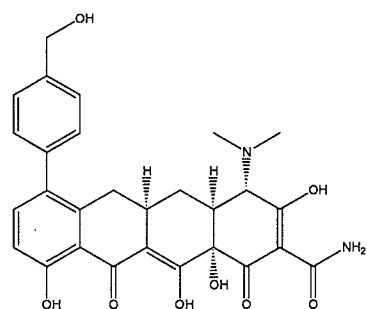
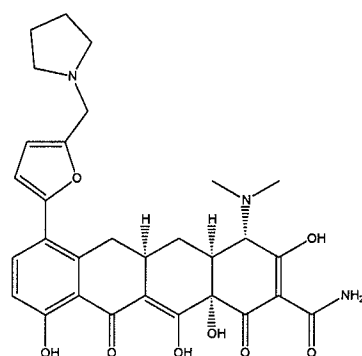
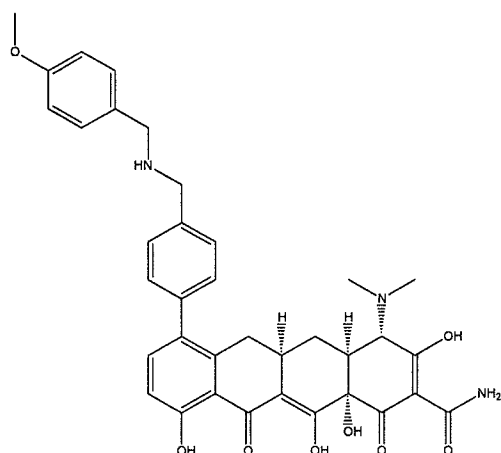


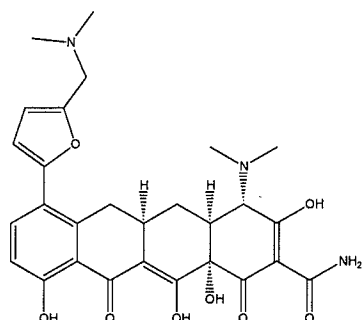
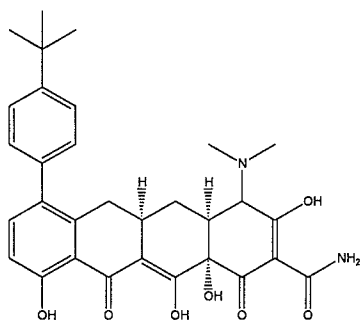
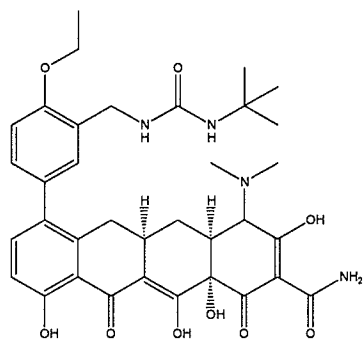
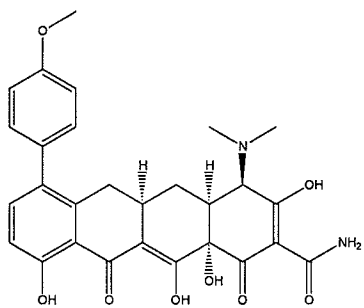
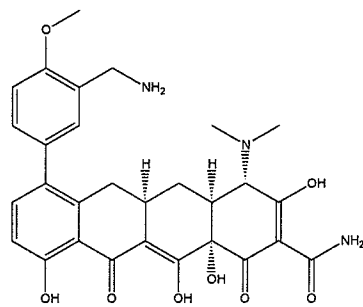
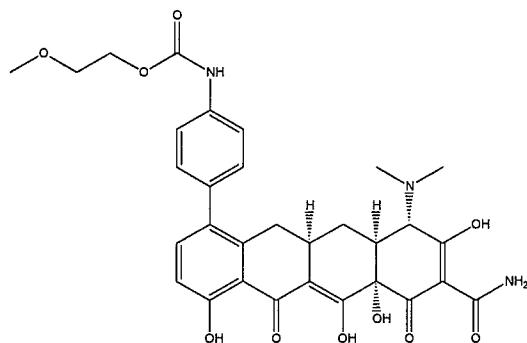
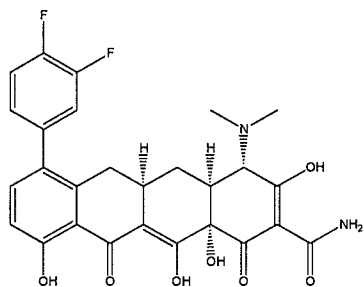


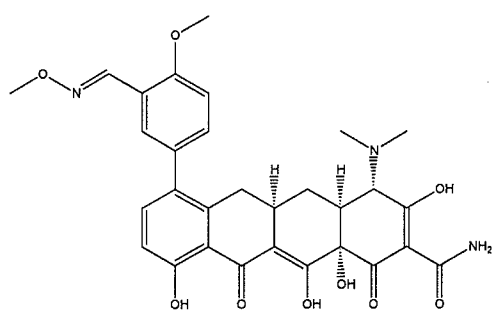
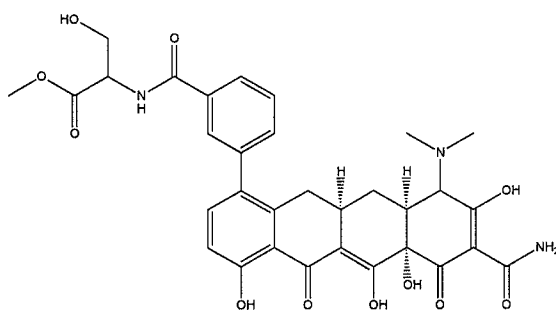
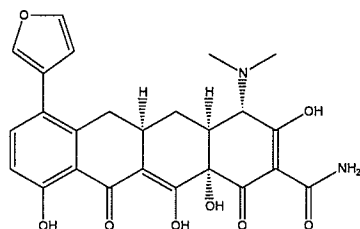
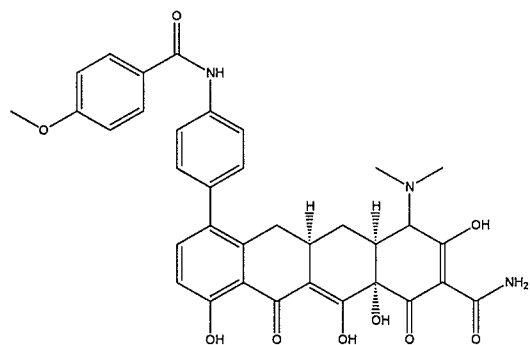
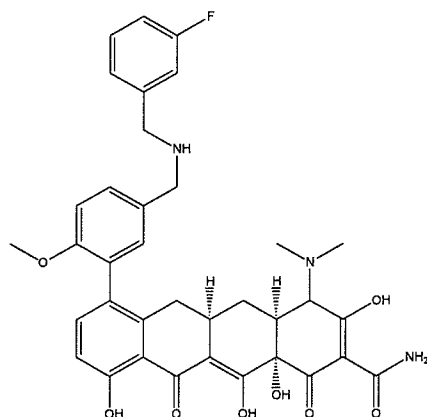
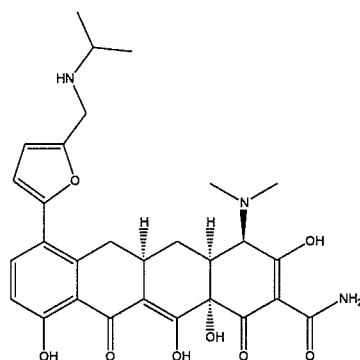
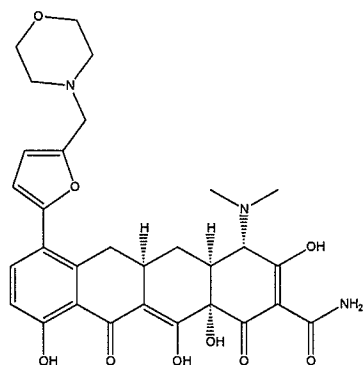


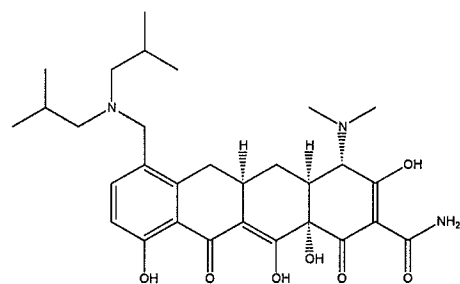
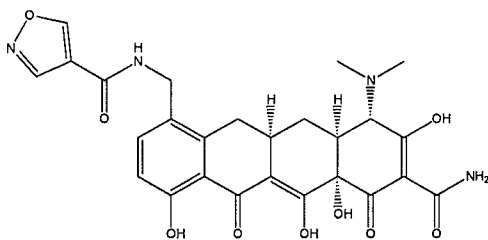
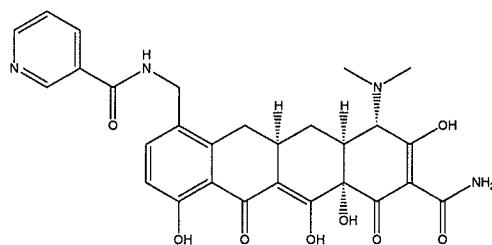
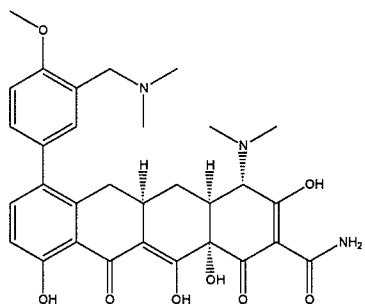
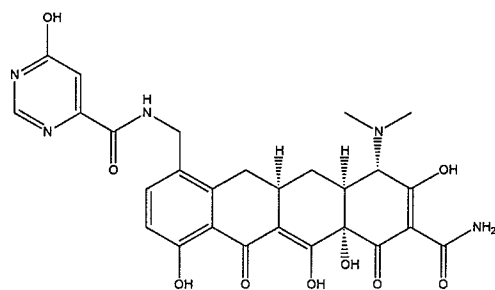
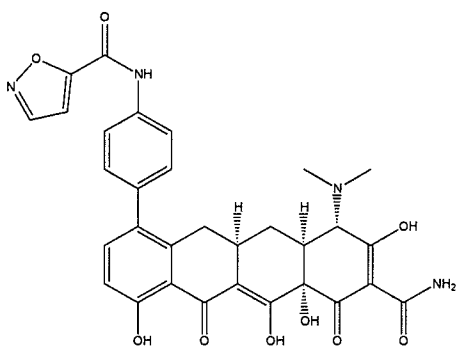
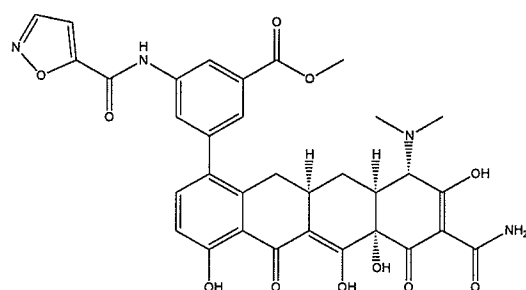
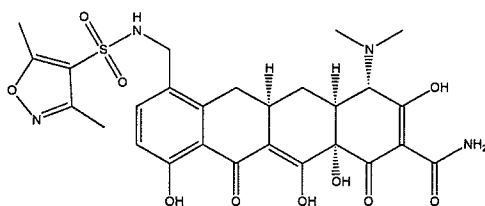
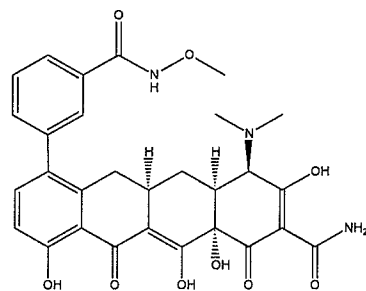
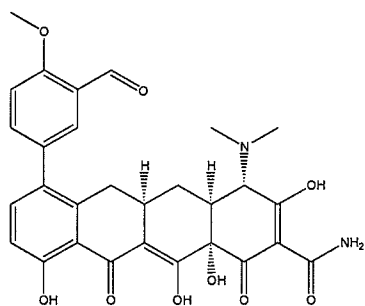


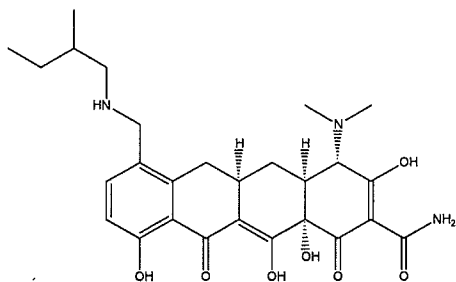
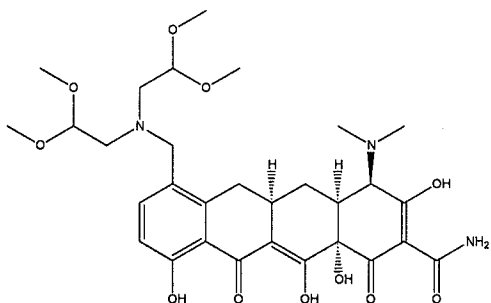
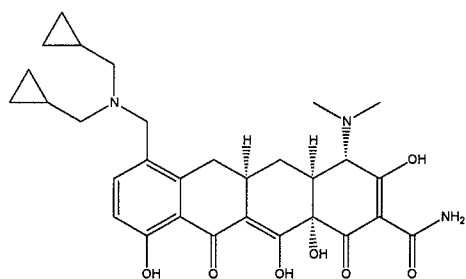
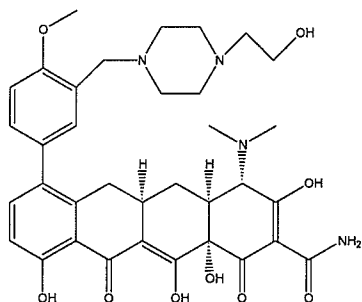
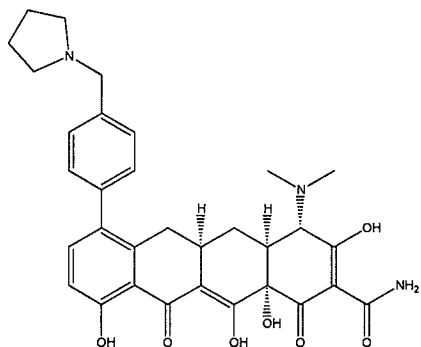
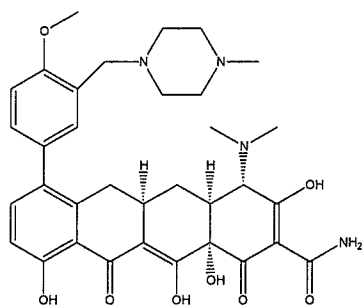
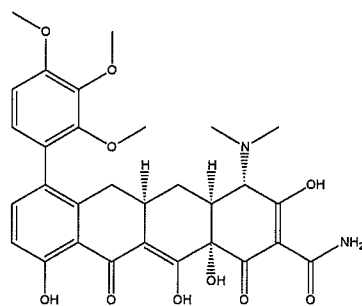
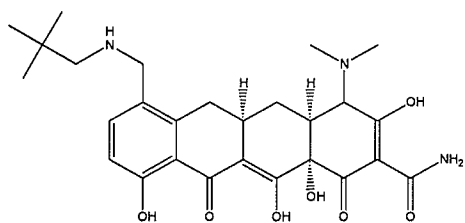


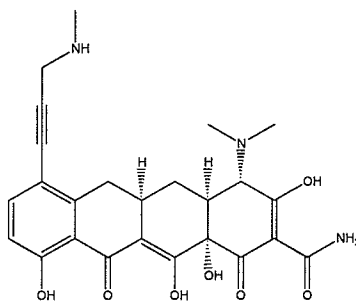
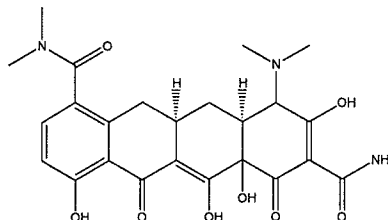
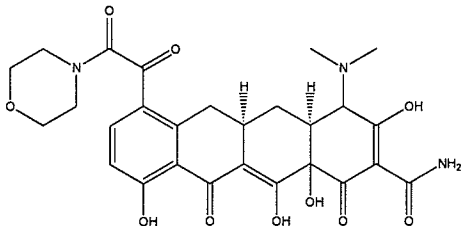
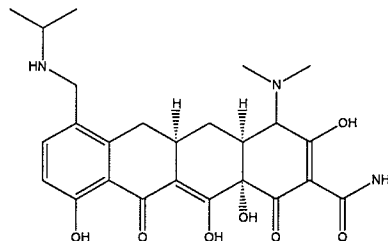
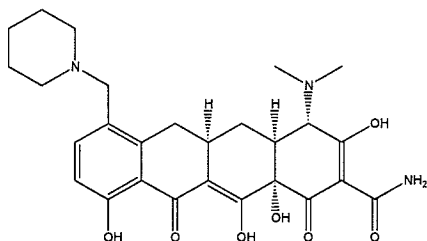
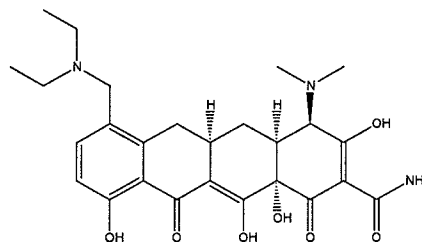
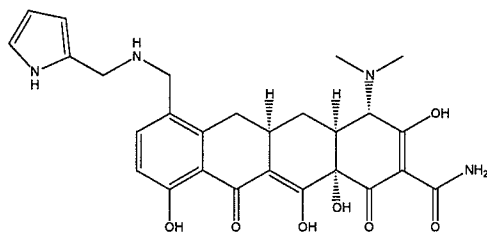
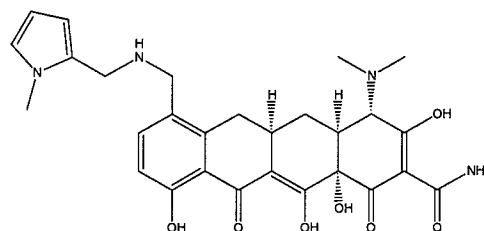
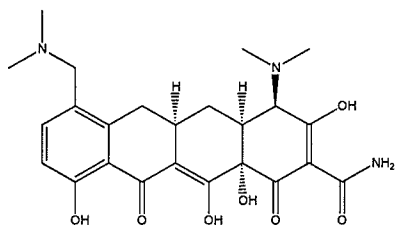


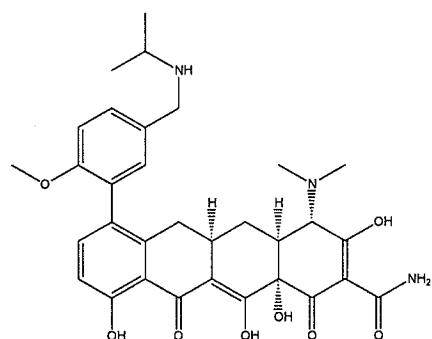
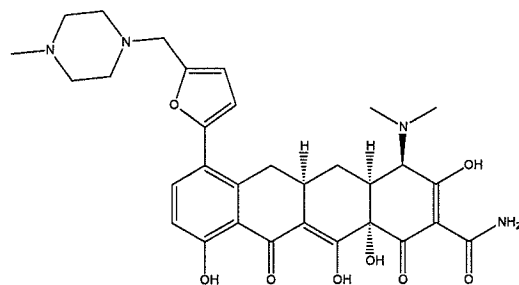
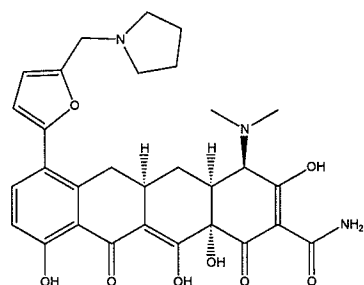
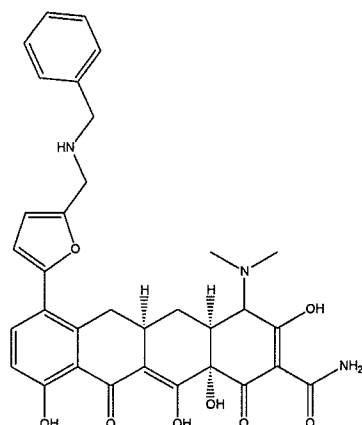
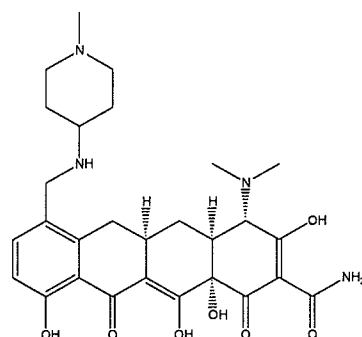
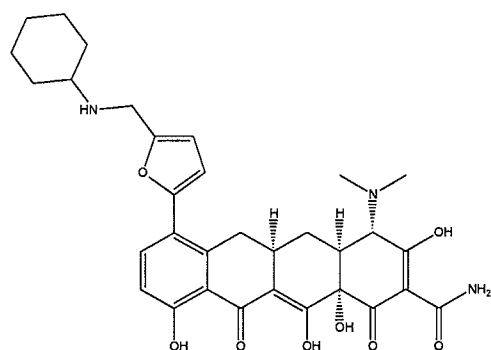


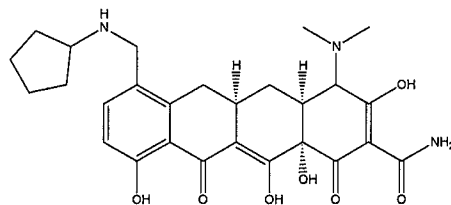
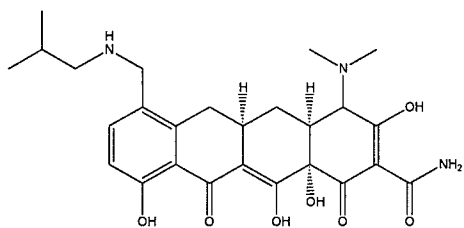
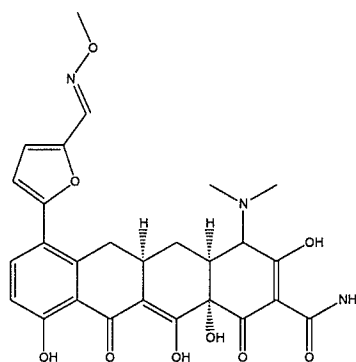
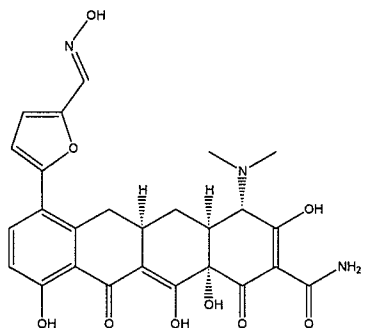
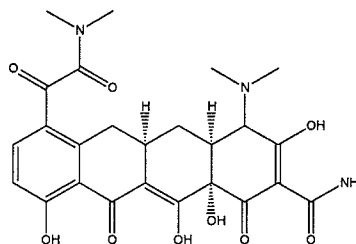
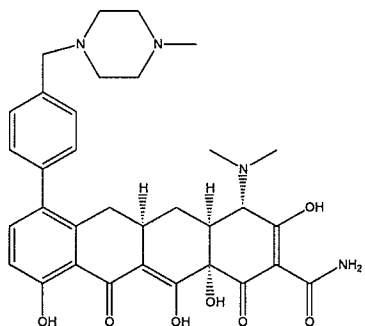
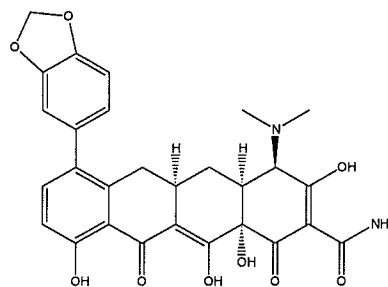
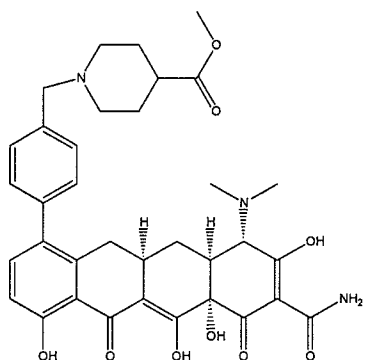


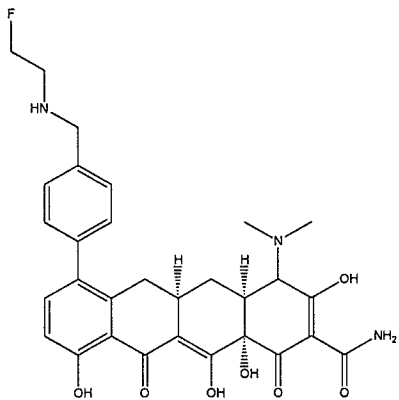
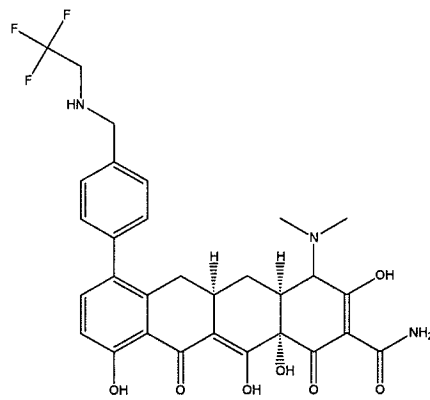
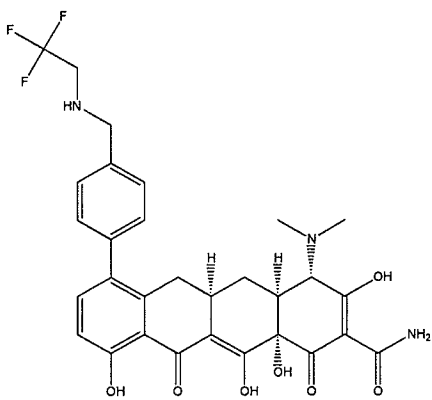
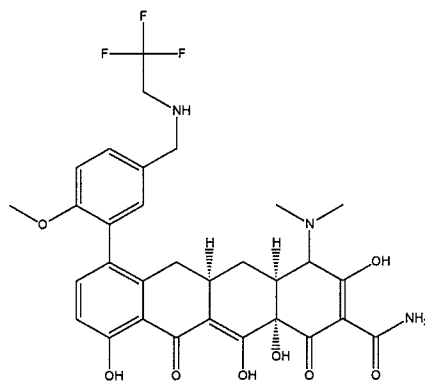
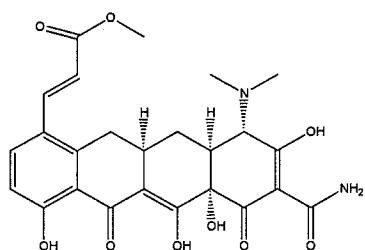


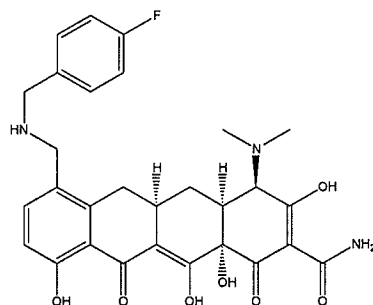
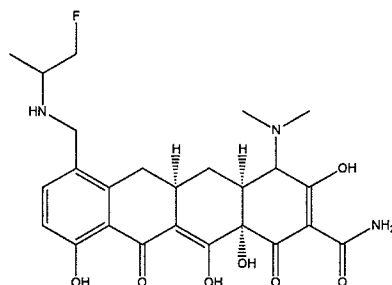
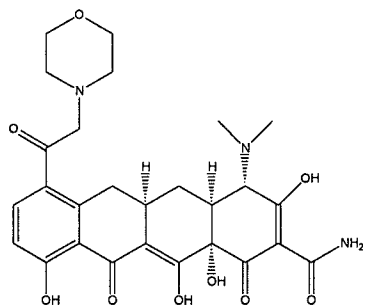
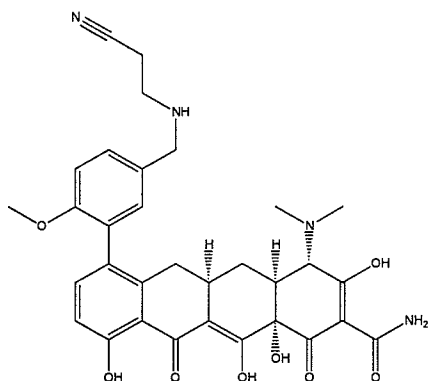
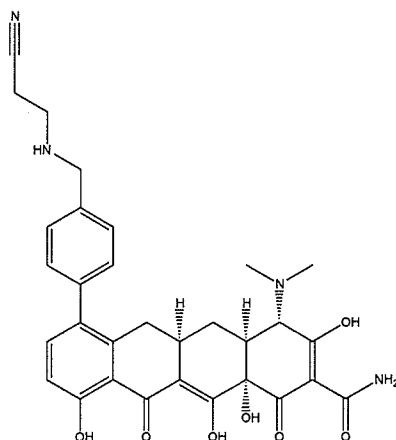
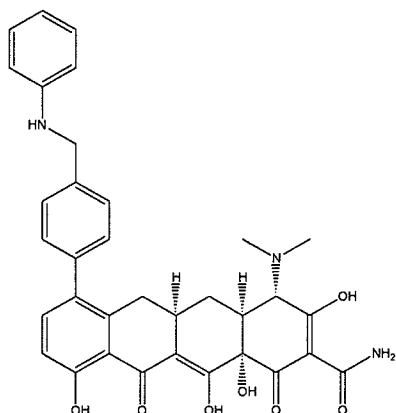


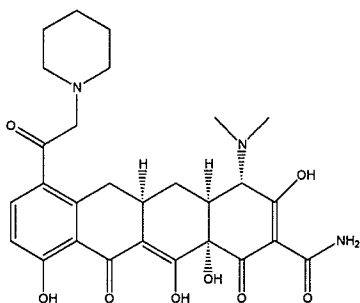
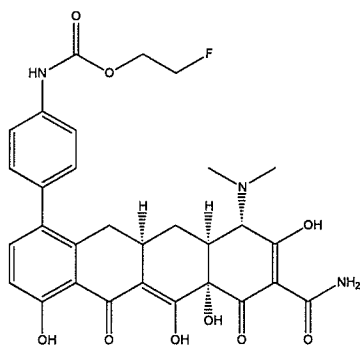
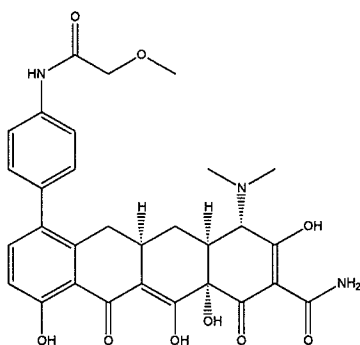
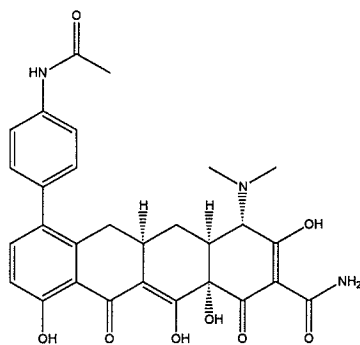
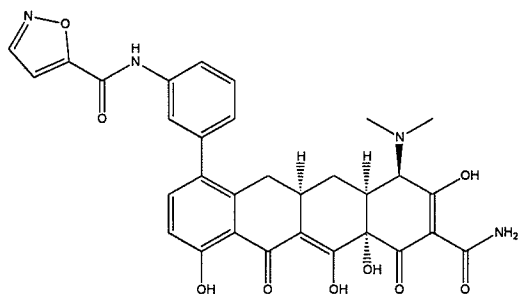
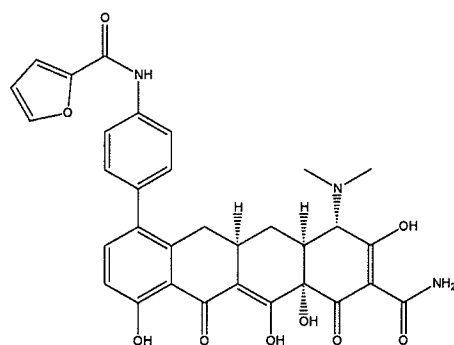
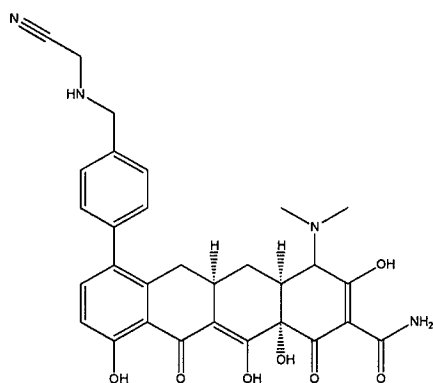


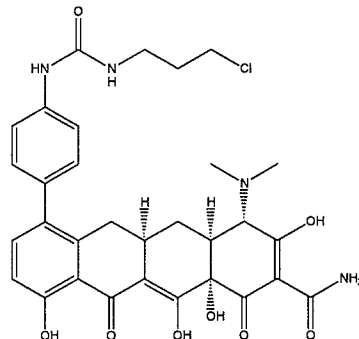
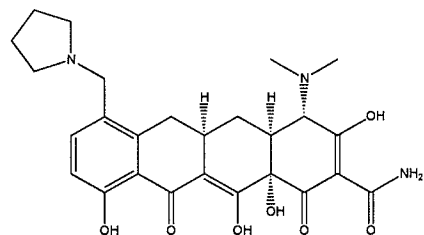
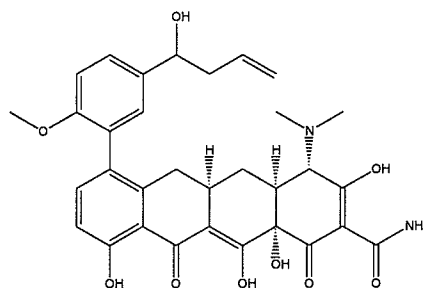
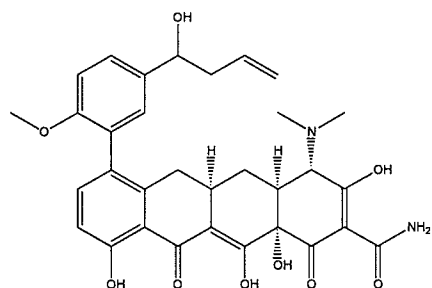
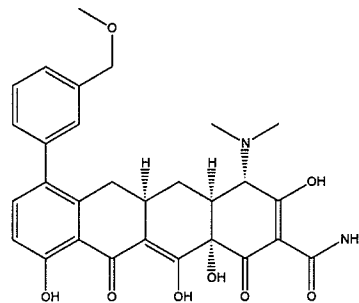
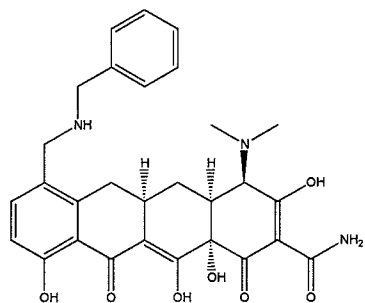
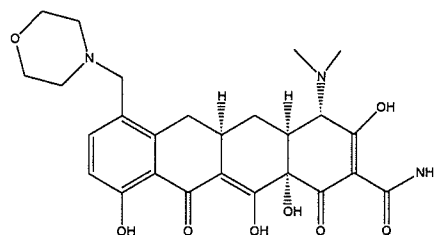
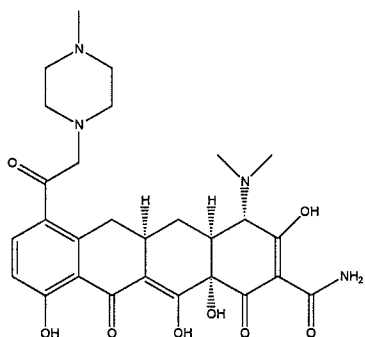


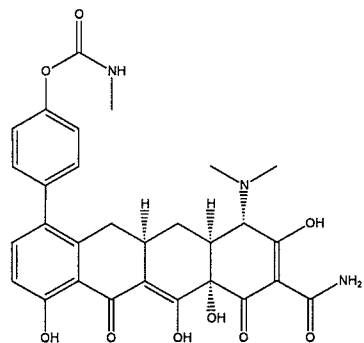
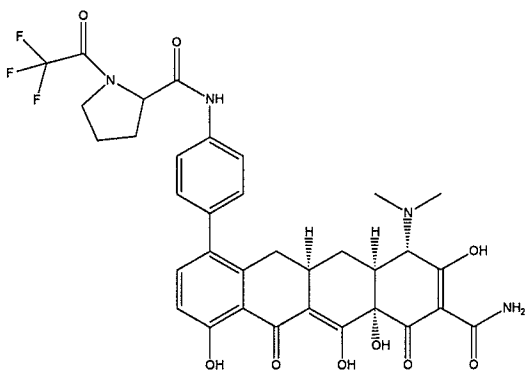
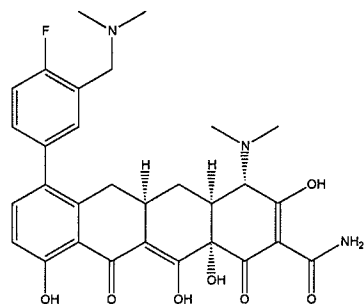
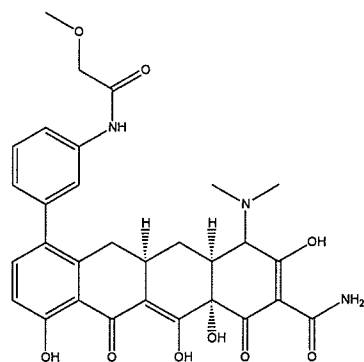
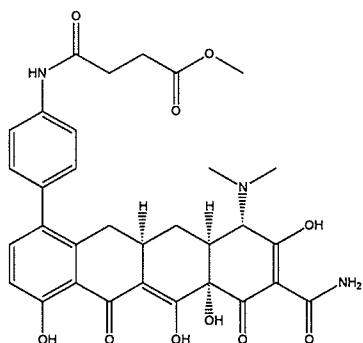
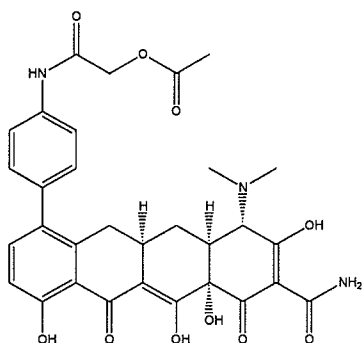


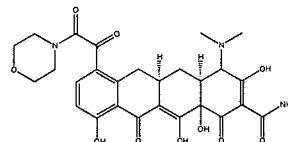
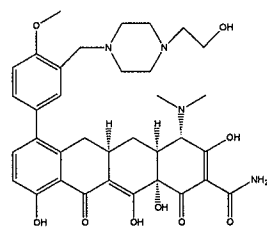
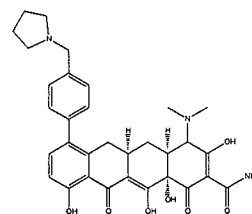
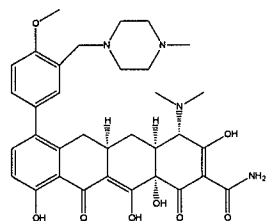
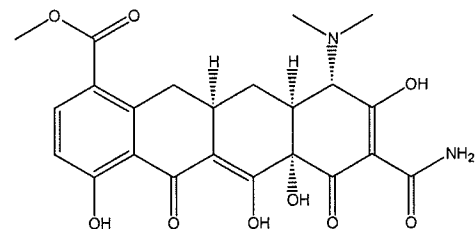
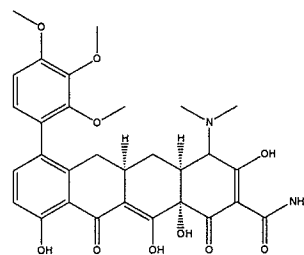
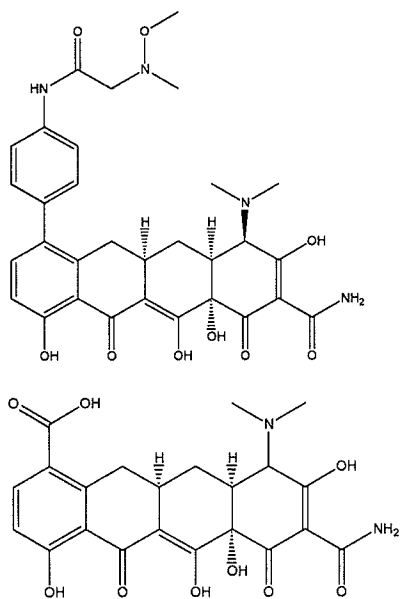


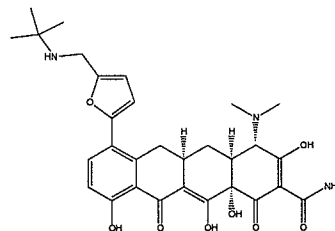
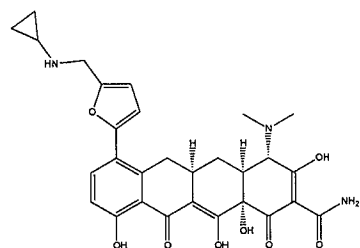
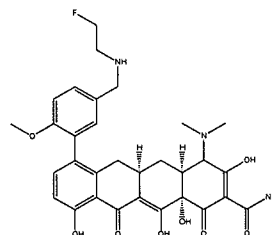
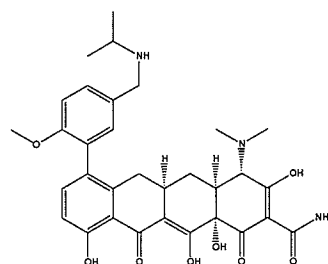
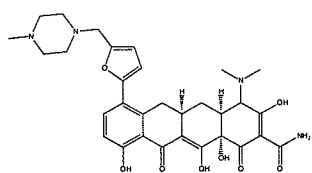
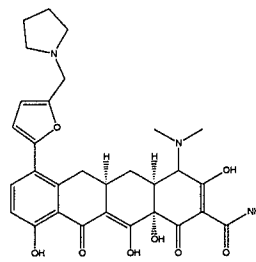
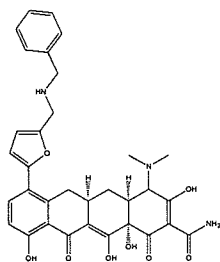
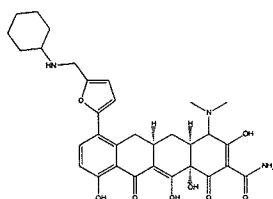
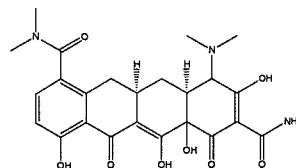
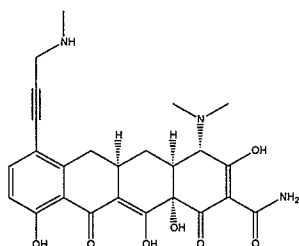


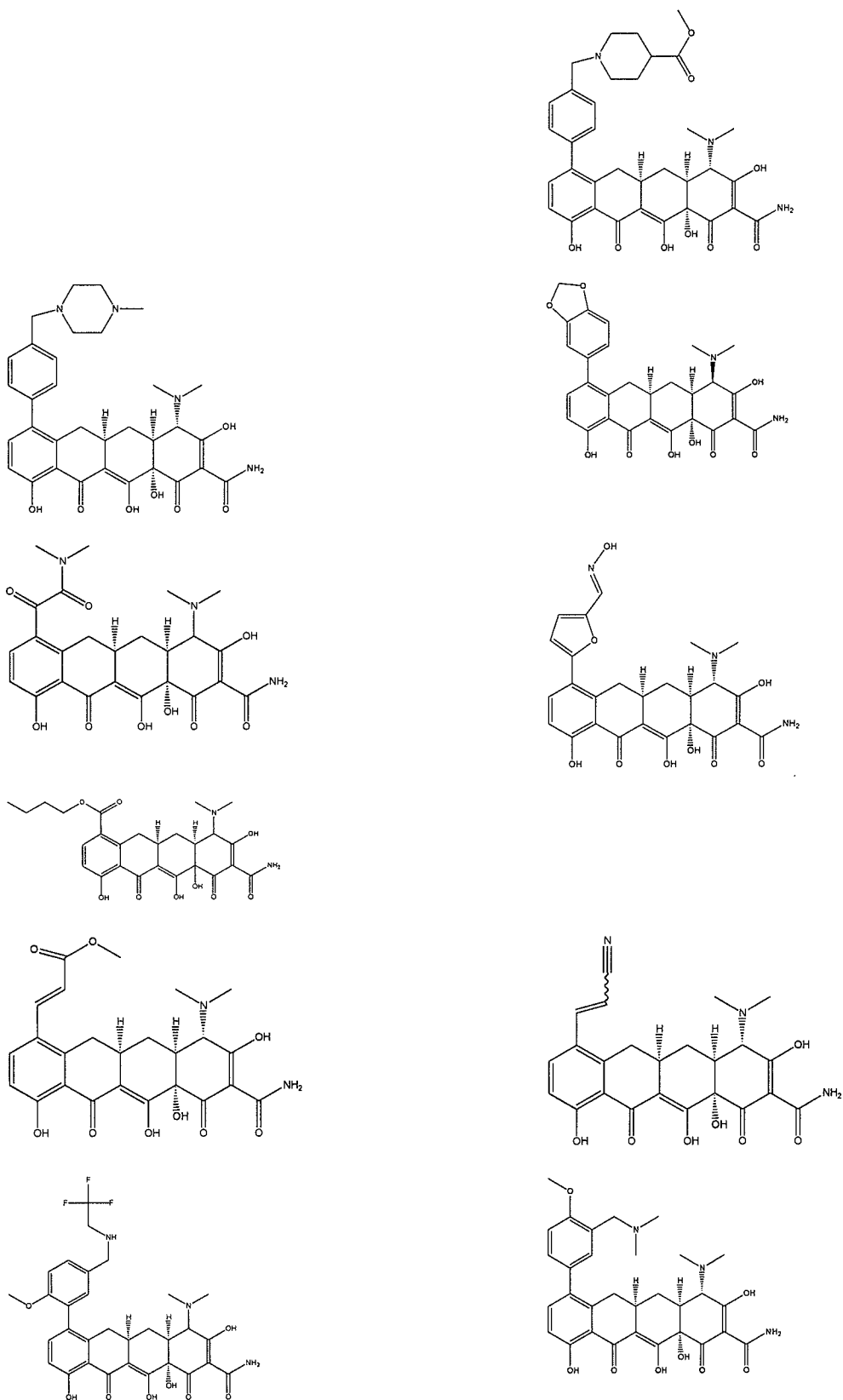


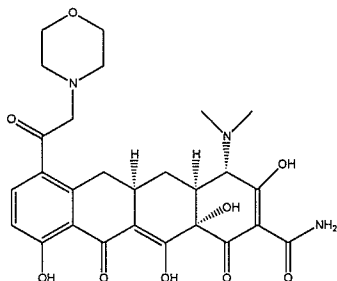
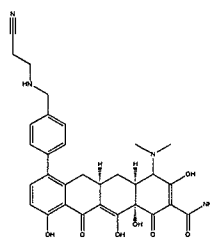
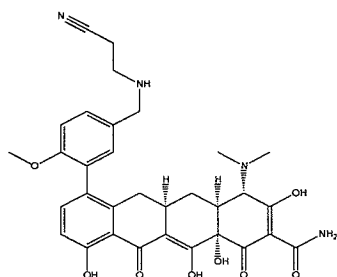
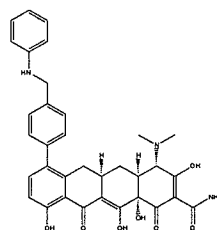
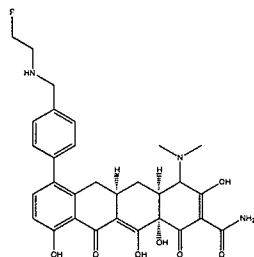
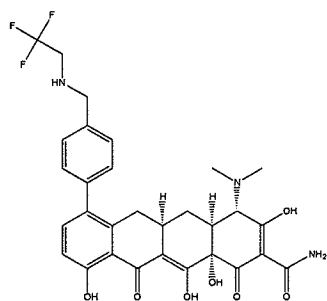
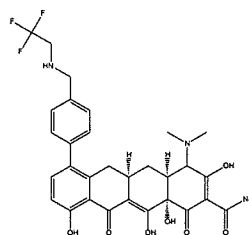
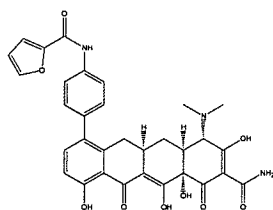


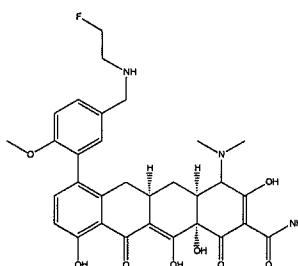
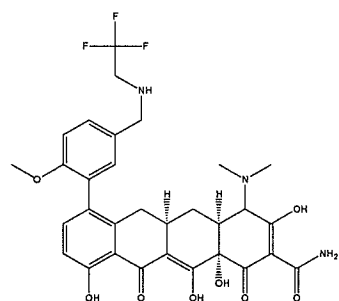
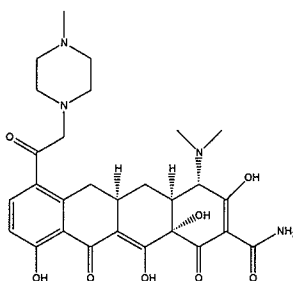
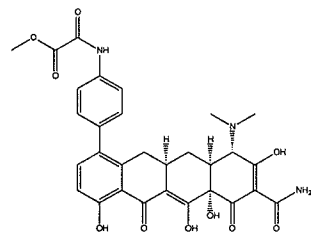
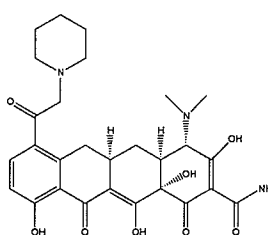
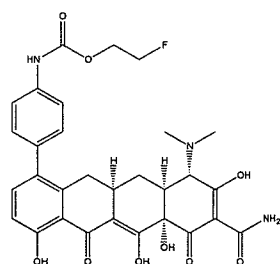
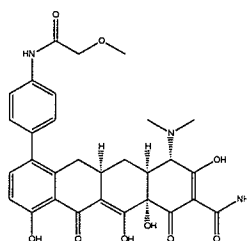
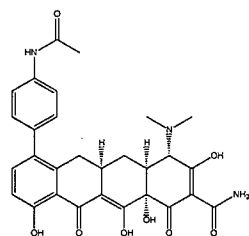
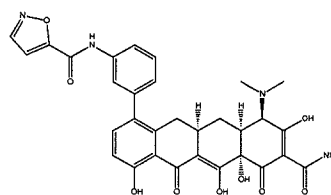
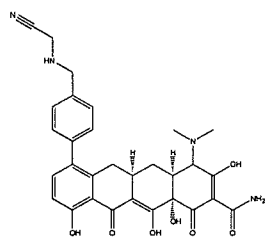


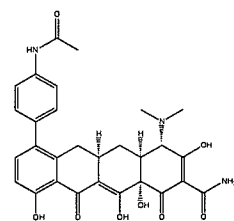
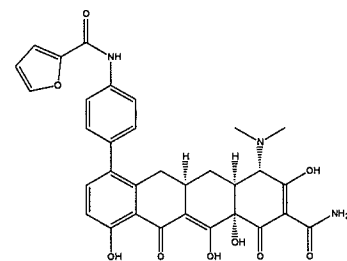
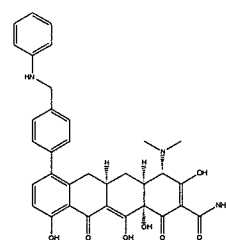
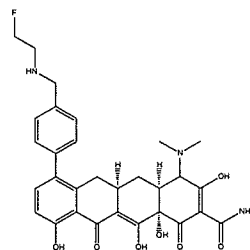
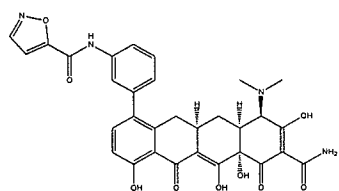
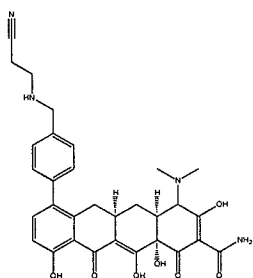
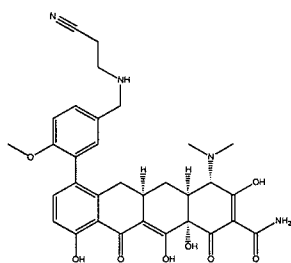
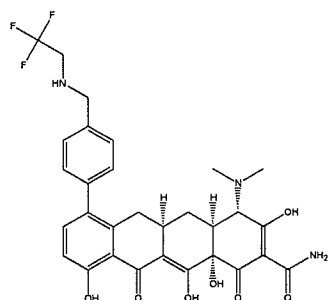
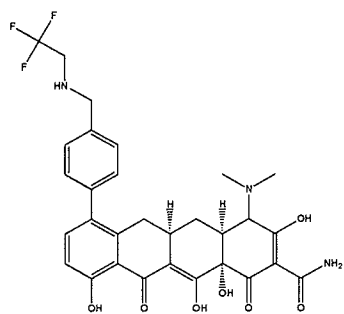


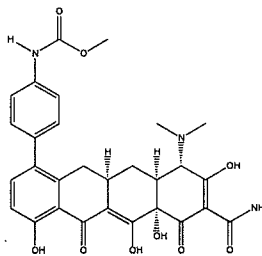
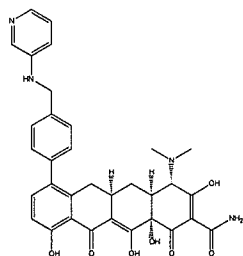
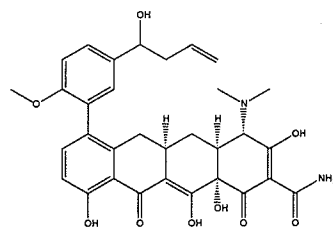
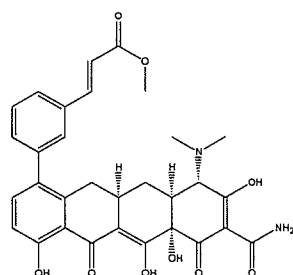
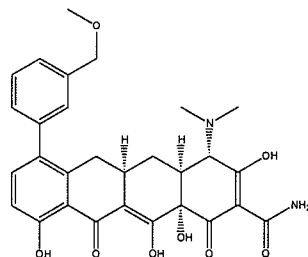
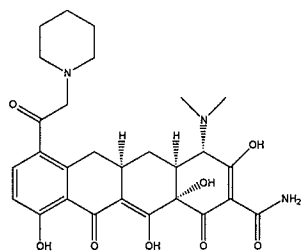
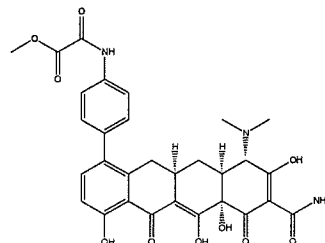
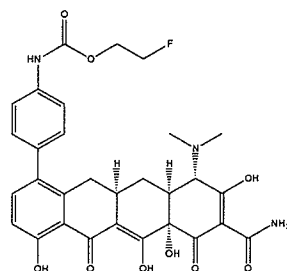
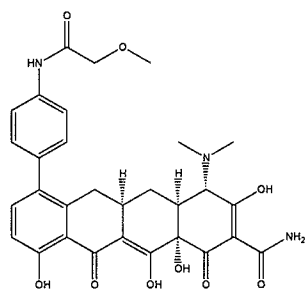


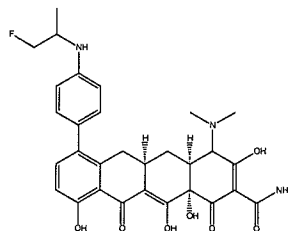
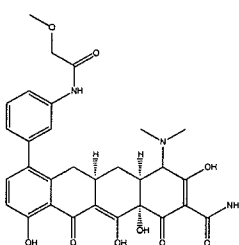
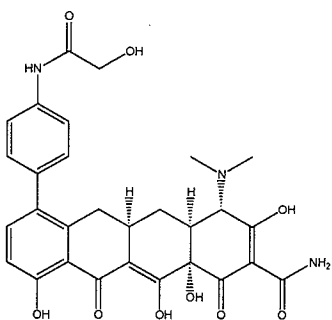
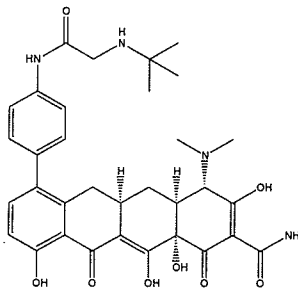
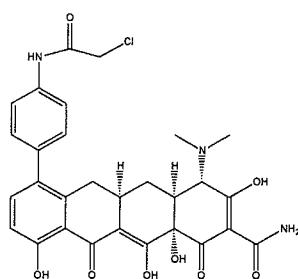
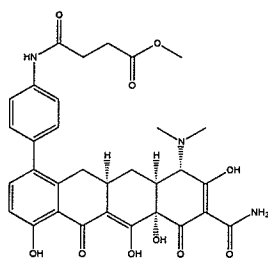
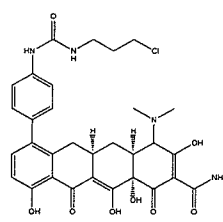
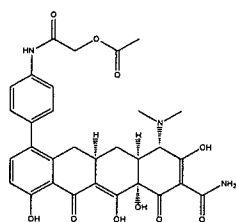


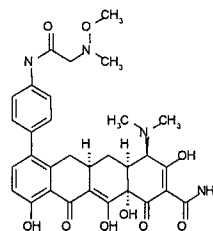
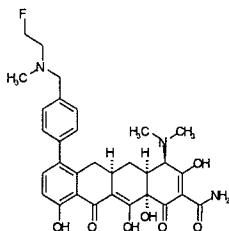
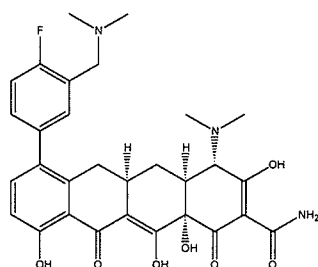
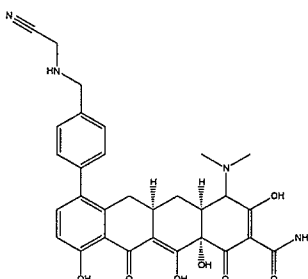
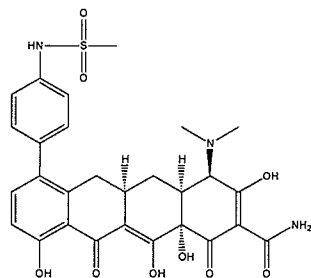
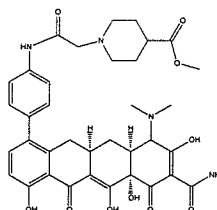
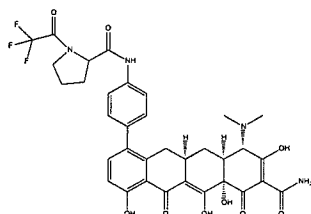
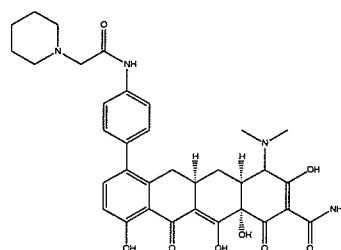
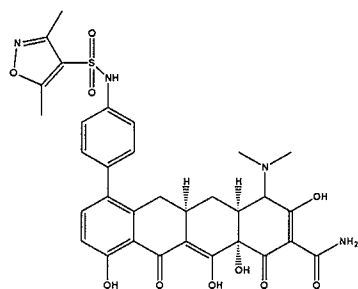


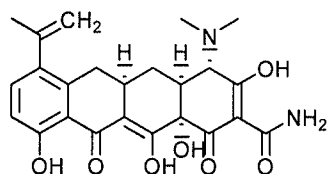
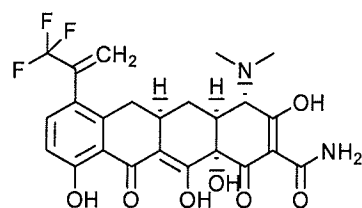
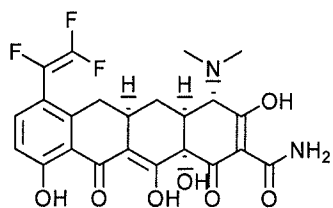
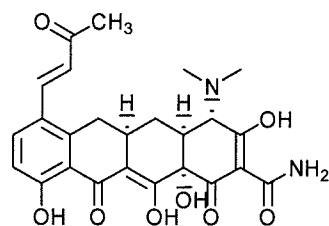
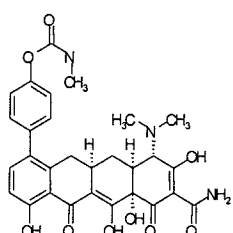
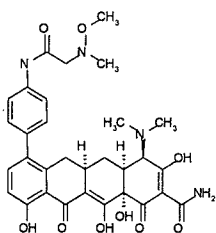
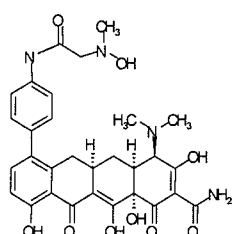
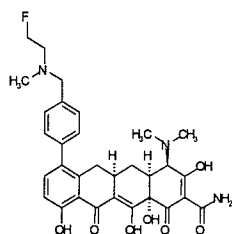
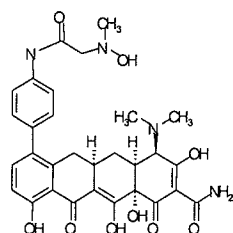
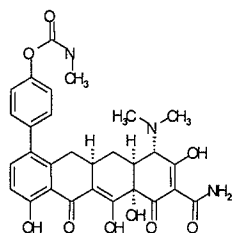


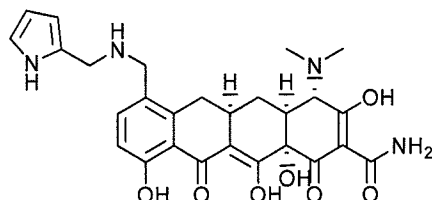
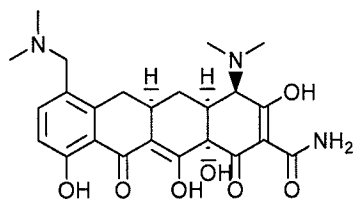
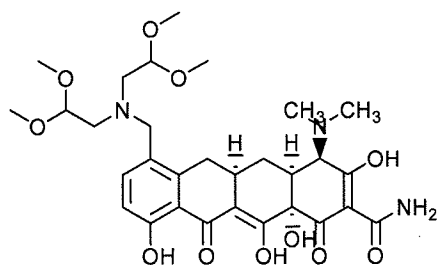
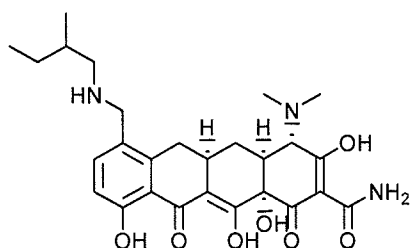
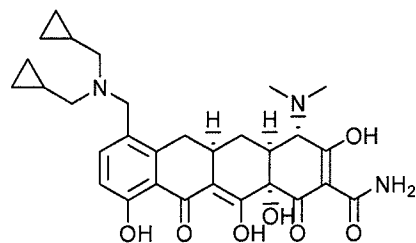
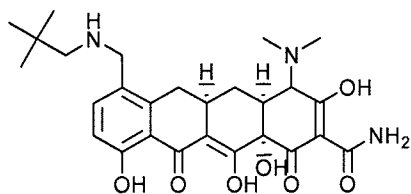
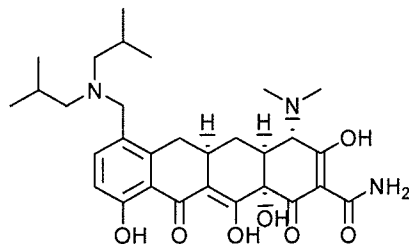
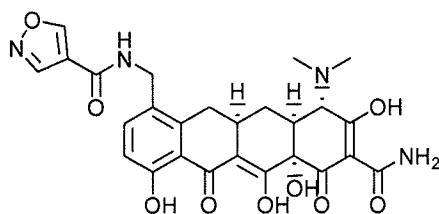
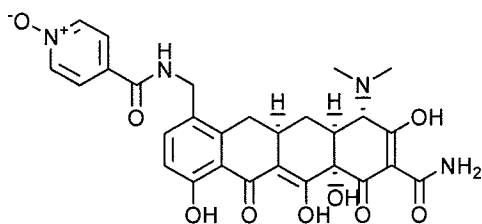
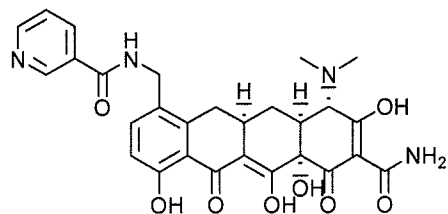
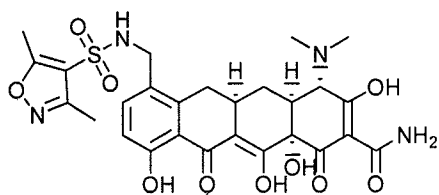


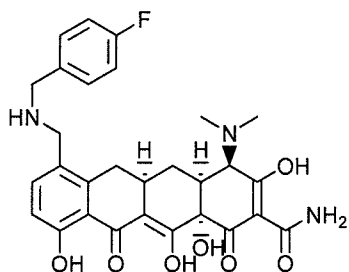
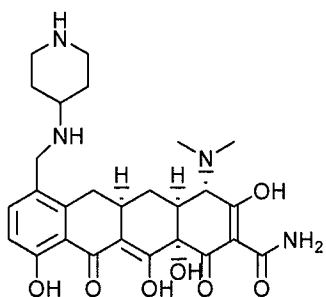
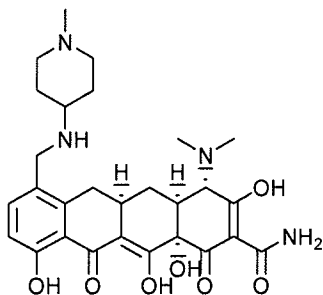
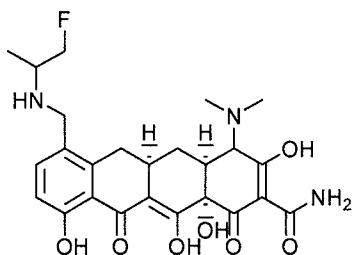
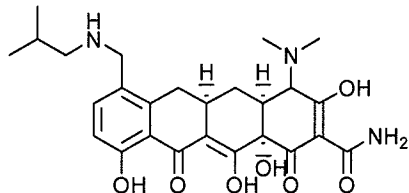
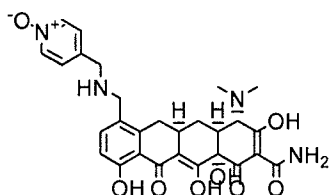
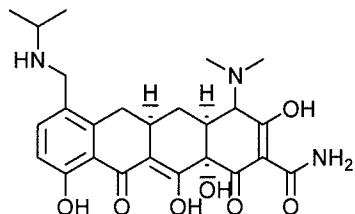
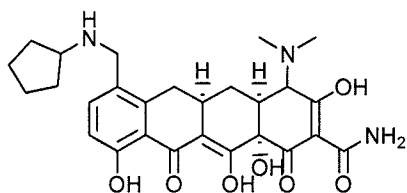
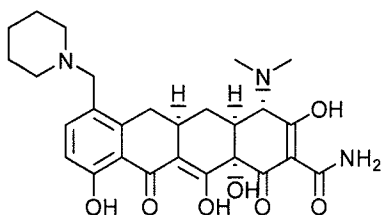
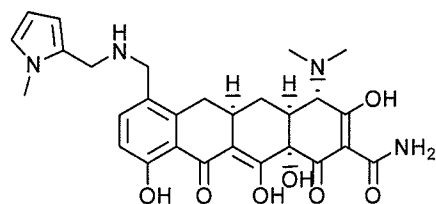
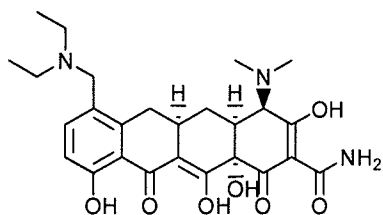


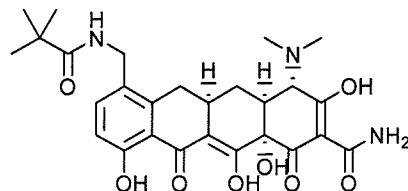
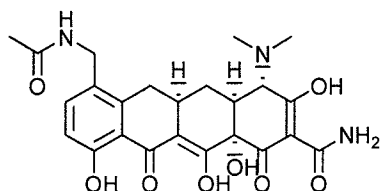
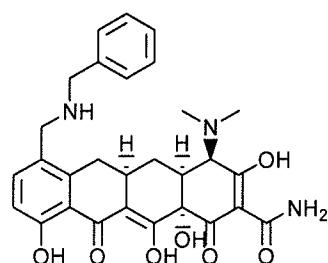
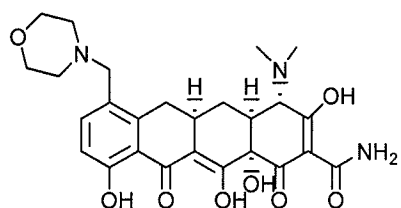












and pharmaceutically acceptable salts, esters and enantiomers thereof; such that said DTMR associated with splicing of nuclear RNA is treated, wherein said DTMR associated with splicing of nuclear RNA is spinal muscular atrophy, and further wherein said effective amount is effective to modulate splicing of said subject's nuclear RNA.